ANALYSIS OF CLINICAL AND INVESTIGATORY PROFILE IN THE MANAGEMENT AND OUTCOME OF GUILLAIN – BARRE SYNDROME

Dissertation submitted to

THE TAMILNADU DR.MGR MEDICAL UNIVERSITY

In partial fulfillment of the requirements

For the award of degree of

DM (NEUROLOGY) – BRANCH-1

MADRAS MEDICAL COLLEGE

THE TAMILNADU Dr.M.G.R.MEDICAL UNIVERSITY
CHENNAI.

AUGUST 2014

CERTIFICATE

This is to certify that the dissertation entitled **"ANALYSIS OF CLINICAL AND INVESTIGATORY PROFILE IN THE MANAGEMENT AND OUTCOME OF GUILLAIN – BARRE SYNDROME"** is a bonafide record of work done by **Dr. GANESA PANDIAN .D** in the Institute of Neurology, Rajiv Gandhi Government General Hospital & **MADRAS MEDICAL COLLEGE**, CHENNAI in partial fulfillment of the Tamilnadu Dr.MGR Medical University rules and regulations for the award of **D.M. (NEUROLOGY)** degree under my direct guidance and supervision during the academic year 2011-2014.

Prof. Dr. S. BALASUBRAMANIAN, M.D., D.M.,
Professor of Neurology,
Institute of Neurology,
Madras Medical College,
Chennai-3

Prof. Dr. K. MAHESHWAR, M.S, M.Ch.,
Professor and Head of the Department,
Institute of Neurology,
Madras Medical College,
Chennai-3

Prof. Dr.R.VIMALA, M.D
The Dean,
Madras Medical College,
Chennai-3.

DECLARATION

I solemnly declare that this dissertation titled **"ANALYSIS OF CLINICAL AND INVESTIGATORY PROFILE IN THE MANAGEMENT AND OUTCOME OF GUILLAIN – BARRE SYNDROME"** is done by me in the Institute of Neurology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai under the guidance and supervision of **Prof. Dr. S. BALASUBRAMANIAN, M.D., D.M.,** Professor of Neurology, Institute of Neurology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai. This dissertation is submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the university requirements for the award of the degree of D.M. Neurology.

Place : Chennai
Date :

Dr. GANESA PANDIAN .D
Student,
Institute of Neurology,
Madras Medical College,
Chennai-3.

ACKNOWLEDGEMENT

I am grateful to **Dr.R.VIMALA,MD.**, Dean, Rajiv Gandhi Government General hospital, Madras Medical College, Chennai, for permitting me to utilize the hospital facilities in conducting this study.

I owe my gratitude to **Prof.Dr.K.MAHESHWAR,MS.,Mch**.,Professor of Neuro surgery, Head of the Department, Institute of neurology, Rajiv Gandhi Government General hospital, Madras Medical College who arranged the necessary facilities to carry out this study and guidance to complete the study.

I am deeply indebted to respected and beloved chief **Prof. Dr.S. BALASUBRAMANIAN**, **M.D., DM.,** Professor of Neurology for her kind and able guidance, inspiration, constant support and encouragement throughout the period of the study.

I express my sincere thanks and gratitude to our Professors, **Prof. Dr. K. Bhanu, Dip. NB., DM., Prof. Dr. G. Sarala, MD., DM., Prof. Dr. R. Lakshmi Narasimhan, MD., DM., DNB.,** and **Prof. Dr. V.Kamaraj, MD., DM**., for their valuable suggestions and support.

I am thankful to all my **Assistant Professors** for their valuable guidance, timely advice and support.

I wish to express my sincere thanks to all the patients who willingly co-operated with me during the course of this study.

Above all, I thank the Almighty Lord God for enabling me to complete this study.

CONTENTS

INTRODUCTION

Guillain-Barre Syndrome (GBS) or Acute Inflammatory Demyelinating Polyradiculoneuropathy is an acute onset, immune-mediated demyelinating disorder of the peripheral nervous system. The aetiology is thought to be widespread demyelination of the spinal roots and the peripheral nerves due to a cross reaction between target antigen and myelin, axon or both. Typical clinical features of GBS are progressive, symmetric muscle weakness associated with absent or depressed deep tendon reflexes. The disorder is heterogeneous and diverse in its antecedent events, clinical presentations and natural course. Although GBS often has a benign prognosis, 7% of patients die and further 16% suffer from residual disability. The modalities of treatment of GBS are supportive treatment, ventilator management, plasma exchange and immunoglobulins.

This study was undertaken to study the clinical and investigatory profile of Guillain Barre Syndrome in Rajiv Gandhi Govt. General hospital, Chennai-3 and in an to attempt to correlate certain clinical and electrophysiological features with prognosis, to identify a poor outcome group in the early stages

AIMS & OBJECTIVES

1. To analyse the clinical profile of GBS
2. To study the prognosis in GBS with reference to:
    a) Age.
    b) Time taken to develop peak deficit from onset (in days).
    c) Duration of plateau phase.
    d) Time taken to onset of improvement.
    e) Requirement of ventilatory support
    f) Cerebrospinal fluid analysis
    g) Nerve conduction study

REVIEW OF LITERATURE

DEFINITION:

Guillain Barre Syndrome (GBS) is a relatively symmetrical, predominantly motor neuropathy, frequently involving facial and other cranial motor nerves with partial or total are flexia for which no specific cause can be demonstrated, although it is commonly preceded by a viral infection. It reaches a peak of disability within four weeks and follows a monophasic course with recovery.

HISTORICAL BACKGROUND

Octave Landry is credited with the earliest description of what is now recognized as GBS. In 1859 he described a condition called 'acute ascending paralysis'. Eichorst in 1877 and Leyden in 1880 described the lymphocytic inflammation of nerve in some cases of peripheral neuropathy.

In 1916, Guillain, Barre, and Strohl - French army neurologists, reported on two soldiers who developed an acute paralysis associated with the loss of muscle- stretch reflexes. They also described an elevation of CSF protein with a normal cell count (albuminiocytological dissociation). Andre Strohl was responsible for the electrophysiological aspects. In 1949, Haymaker and Kernohan described the clinical and histopathological features, including

inflammatory changes of the peripheral nerve in 50 fatal cases of GBS. In the mid-1950s, Waksman and Adams produced experimental allergic neuritis in animals by injection of homologous or heterologus peripheral nerve tissue combined with Freund adjuvant.

Landry's paralysis and Guillain Barre Syndrome were thought to be different entities (with a benign prognosis for GBS and an ominous prognosis for Landry's paralysis) till Haymaker and Kernohan in 1949, exhaustively reviewed this debate and entitled their paper Landry-Guillain-Barre syndrome implying that the two condition are identical

C. Miller Fisher in 1956 observed a variant associated with ophthalmoplegia, ataxiaand areflexia. In the 1980s, plama exchange was found to be an effective treatment, and in the 1990s, efficacy was also demonstrated for intravenous immunoglobulins

PATHOLOGY:

GBS is increasingly recognized to encompass several pathophysiological patterns. However the most prevalent form of GBS in most of the world is acute inflammatory demyelinating polyneuropathy (AIDP). This form is characterized pathologically by demyelination and macrophage mediated clearance of myelin. Classically, a perivascular mononuclear inflammatory infiltrate of lymphocytes, monocytes and plasma cells is seen in

endoneurium and myelin sheath. Patchy, segmental, multifocal demyelination is present along peripheral nerves, including nerve roots, whereas the axons themselves are relatively spared except in the more severe cases. This abnormality is prominent around ventral roots and in the plexus and proximal nerve trunks, but may, in some are associated with a higher incidence of antibodies to ganglioside GM-1 and Campylobacter infection.

PATHOGENESIS :

The pathogenesis of GBS remains incompletely understood, but it is an autoimmune disorder that can often be linked to an antecedent infection. The autoimmune hypothesis of GBS is based largely on the close correlation between GBS and experimental allergic neuritis (EAN), and the failure to associate any single infectious agent with the diseases. Also, failure to associate autoimmune response to any defined peripheral myelin autoantigen, raises the possibility that a number of autoantigens may be involved.

EAN, induced by immunizing rabbits or guinea pigs with peripheral nerve is produced by inoculation with myelin and a species-specific antigen or its fragments. The experimental disease appears to be predominantly cell mediated.

Thus, current work supports the concept of a primary lymphocytic cell mediated mechanism for inflammation in GBS, presumably as an aberrant

response to a precipitating infection or other immunological stimulus. Activated T- cells expressing several surface receptors circulate during the active illness and serum levels of interleukin-2 and its soluble receptor are greatly increased. Some T-cells are sensitized to P-2, a major peripheral nerve myelin antigen, but specificity of this response is unclear.

Humoral factors including both antibodies and complement may also play a role in GBS as evidenced by efficacy of plasmapheresis in the complement activation products C3a and C5a in the CSF, soluble C5b-9 complexes in serum and CSF, and deposits of complement and IgM on myelin sheaths in biopsy specimens from patients with GBS.

Circulating antineural antibodies against a number of antigens have been demonstrated in GBS including against P-2 protein of nerve myelin and a variety of glycoconjugates like GM-1, GD 1b, asialo -GM1, SGPG and sulfatide.

A causal link between a preceding infection and GBS has been constructed based on concept of molecular mimicry. An autoimmune response initially launched against the invading organism would secondarily produce damage to peripheral nerve.

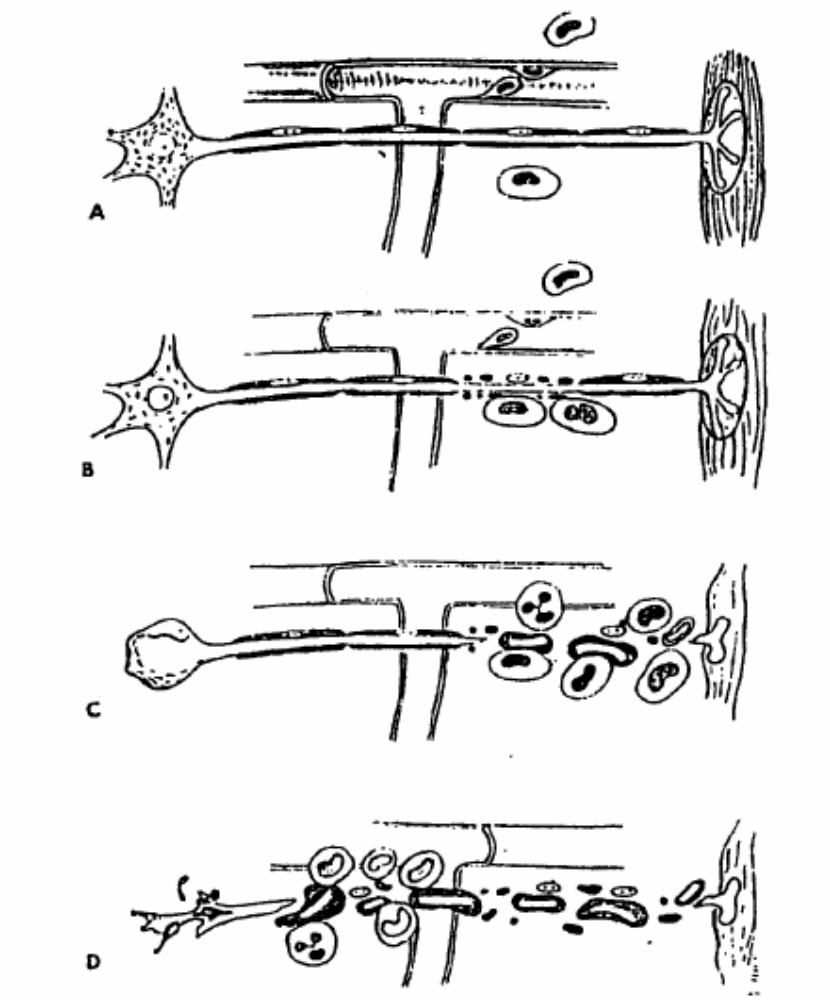


Fig. 1 : Diagrammatic representation of probable cellular events during GB5.

A) Lymphocytes attach to the walls of endoneural vessels and migrate through the vessel wall, enlarging and transforming as they go. At this point, no nerve damage has occurred; myelin and axons are intact.

B) More lymphocytes have migrated from the vessel lumen into the surrounding tissue, and macrophages have made their appearance. The first visible morphologic effect is segmental demyelination i.e., breakdown of

myelin with sparing of the axon. Segmental demyelination is by far the most common structural change in nerve fibres in GBS.

C) The lesion is more intense, and, as a result, there is interruption of the axon in addition to myelin sheath damage. Polymorphonuclear leukocytes are present as well as lymphocytes and macrophages. Because the axon is interrupted, the muscle undergoes denervation atrophy, and the nerve cell body shows the changes of central chromatolysis.

D) If axonal damage has occurred proximally because of a particularly intense root or proximal nerve lesion, the nerve cell body may die and undergo dissolution. In this situation, there is no hope of regeneration, although there is presumably the possibility of collateral reinnervation of muscle from surviving motor fibers.

ANTECEDENT EVENTS :

A variety of antecedent events have been noted to precede onset of GBS. In one study of Ropper et al at Massachusetts General Hospital, 27% had no prior identifiable illness or antecedent event, 49% had an upper respiratory infection, 10% had a diarrhoeal illness, 3% had some form of pneumonia, 3% had Epstein-Barr virus, 3 % had cytomegalovirus infection, 3% general malaise noted and 3% had miscellaneous events including Hodgkin's disease, surgery, systemic lupus, or vaccination.

Approximately two thirds of cases of GBS follow an infection, usually viral including HIV, Cytomegalovirus or Epstein Barr virus with hepatitis or mononucleosis. Asymptomatic hepatitis, presumably viral, has also been seen. GBS has been reported to follow all the common childhood viral diseases, including measles, chicken pox, rubella, mumps and influenza A and B infections. Campylobacter jejuni enteritis has been recently recognized as an important preliminary illness, often associated with severe or variant forms of neuropathy.

Vaccination of various types, general surgery, epidural anaesthesia, and drugs, including thrombolytic agents and heroin have been associated with a few cases. After much debate, the incidence has favoured a slight increase in cases of GBS attributable to the inoculation programme for swine influenza in 1976. GBS is an occasional complication of rabies vaccination 16, especially with neural tissue containing vaccines. The median time from the first injection to onset of neuropathic symptoms is 11 - 15 days. Those cases with the shortest incubation period tend to be the most severe. Only a few cases of the syndrome have been reported following duck embryo rabies vaccine or human diploid cell rabies vaccine. An association with typhoid vaccine and tetanus toxoid is possible. However association with other vaccines remains doubtful at present.

A small category of GBS occurs in the presence of an underlying systemic disease, most commonly systemic lupus erythematosus (SLE), Hodgkin's disease (and less frequently other neoplasia), Sarcoidosis or recently acquired HIV infection. These occur more frequently in patients with chronic inflammatory demyelinating polyneuropathy, perhaps because the immune dysfunction is also chronic, rather than monophasic, as in the infections that precede acute GBS. Autoimmune diseases other than SLE are only rarely associated with a demyelinating polyneuropathy but they can cause multiple vasculitic mononeuropathy, immunocompromised patients may acquire GBS, even while they are taking high dose corticosteroids. Lyme disease is not typically associated with GBS, but it causes a similar subacute neuropathy

CLINICAL FEATURES :

Usually, patients experience an acute respiratory or gastrointestinal illness that lasts for days and then resolves. This is followed in 1 to 2 weeks by the development of an 'ascending' paralysis. Typically, GBS begins with fine paresthesiae in the toes or fingertips, followed within days by motor weakness

Weakness:

Typically the legs are involved initially, and within a few days, the arms. Patients will complain of difficulty in walking, trouble in arising from a chair, going up or down stairs, or instability of gait. Limb weakness is

relatively symmetric, and there is symmetric loss of the muscle stretch reflexes. Variable arm, facial and oropharyngeal weakness follows.

Weakness tends to progress, usually over a course of 1 to 3 weeks. 50% patients reach maximal weakness by 1 week, 70% by 2 weeks, and 80% by 3 weeks. Occasionally, fulminant rapidly progressive course occurs, in which paralysis becomes maximal within 1 or 2 days.

In severe cases the disease may progress to affect respiration, eye movements, deglutition, and autonomic functions. About one third of patients develop involvement requiring mechanical ventilation. 50% develop cranial nerve involvement, which is most often facial weakness. One half of patients develop oropharyngeal weakness. And 10% to 20% develop significant autonomic dysfunction (including fluctuations of blood pressure, heart rate, ileus, or urinary retention).

SENSORY

Although symptoms are predominantly motor, sensory disturbances in the form of distal paresthesias and numbness are frequently described by the patient. Typically, GBS begins with fine paresthesiae in the toes or fingertips, followed within days by motor weakness. Pain is common, as either bilateral sciatica or aching pain, similar to the muscle discomfort following exercise, involving the large muscles of the thigh, flanks, or back. However objective sensory deficit is only rarely found. Some patients may have joint position and

vibratory sensation impairment, and stocking-glove deficits to pinprick are occasionally found.

Autonomic dysfunction :

Autonomic neuropathy is a common and important complication and may involve both sympathetic and parasympathetic fibers. While minor autonomic dysfunction probably occurs in a large percentage of cases, significant autonomic dysfunction occurs in 10% to 20% of patients.

Serious cardiovascular dysfunction may present as sustained or episodic hypertension, pronounced blood pressure fluctuations and orthostatic hypotension. The most common abnormality is sustained sinus tachycardia, which usually does not require treatment. Sinus arrhythmia may also be seen. Vagally mediated arrhythmias such as profound bradycardia and cardiac arrest are more ominous and may require atropine and cardiac pacemakers.

Autonomic neuropathy may also involve the sudomotor, gastro-intestinal tract and other systems presenting as excess sweating, constipation or nausea (from reduced bowel motility), urinary retention and impotence.

After the progression of weakness stops, patients tend to plateau for 2 to 4 weeks and then slowly recover. The typical patient becomes bedridden with distal paresthesias, incomplete bilateral weakness of facial muscles, some difficulty in swallowing, and a vital capacity that is about half of the predicted

value. In the mildest cases, the patient can still rise from a kneeling position and walk on the heels and and toes whereas in the worst cases the patient is quadriplegic and ophthalmoplegic and requires mechanical ventilation. However, in most, the recovery is such that by 6 months into the course of illness, 85% of patients are ambulatory.

In 3% of cases there is recurrence of the paralytic illness, although some of these patients may have instead a chronic inflammatory neuropathy, as opposed to recurrent GBS.

Overall, the mortality from the acute illness is 2% to 5%. About one half of patients have some degree of long-term residual symptomatic abnormality. 15% to 20% cases have residual motor weakness at 1 year, and 5% remain severely disabled.

VARIANTS :

Of the many various from this typical clinical presentation, the commonest but most aberrant is Miller- Fisher's Syndrome which involves ophthalmoplegia, ataxia and areflexia with little weakness and accounts for 5% of cases in a large series.

The other variants are :

1. Acute sensory loss associated with areflexia and peripheral demyelination. It must be distinguished from acute sensory neuropathy.

2. Acute autonomic neuropathy (acute pandysautonomia) first described by Young and coworkers, may be a variant of GBS, affecting only the autonomic nervous system, but this still remains to be proven.
3. Weakness without paraesthaesiae or sensory loss.
4. Isolated weakness of the arm and oropharynx or of the leg.
5. Acute polyneuritis cranialis not involving the first or second cranial nerves, may be a variant of GBS, when there is a monophasic illness with acute onset, raised CSF protein and recovery and no other cause is found.
6. Bilateral weakness of facial muscles with distal paraesthesia.
7. Axonal GBS with rapid, almost complete paralysis and electrically inexcitable motor nerves.
8. Pharyngeal cervical-Brachial weakness (resembling Botulism or Diphtheria).
9. Paraperesis resembling a spinal cord lesion-areflexic paraperesis sparing power and reflexes in the arms, face, and respiratory muscles throughout the illness
10. Severe ptosis without ophthalmoplegia - severe ptosis of the upper lids with minimal or no opthalmoplegia or iridoplegia, and mild facial weakness early in their illness, progressing to typical GBS of the restricted pharyngeal - cervical - brachial form.

11. Acute severe midline back pain -seen as the first symptom, on waking or beginning paroxysmally after rolling over in bed; the pain was described as excruciating, and was so distracting that the patient screamed repeatedly. The pain abated over two to three days, as a typical GBS including bifacial paresis, evolved.

All are linked to GBS by the regional or global decrease in tendon reflexes, transitional forms of the disease, shared electro-physiological features and elevated concentration of protein in cerebrospinal fluid.

In 1956, C. Miller Fisher reported "an easily recognizable syndrome characterized among other features by total external ophthalmoplegia, severe ataxia and loss of the tendon reflexes". This well recognized variant of GBS has given the eponym of Fisher's syndrome, and accounts for about 5% of the cases of acute GBS in most series.

Patients typically present with diplopia followed within several days by ataxia or clumsiness of the limbs. One half of patients describe paresthesias and some patients describe dizziness. Over the first week of neurological symptoms, patients usually develop hypoactive or absent muscle stretch reflexes. The ophthalmoplegia evolves over 1 to 3 days and is usually severe, complete and relatively symmetric. Most patients have ptosis. Pupillary function tends to be normal. Occasionally, other cranial nerves are involved,

resulting in oropharyngeal or facial weakness. About one third of the patients develop associated severe limb weakness with respiratory failure.

The presence of ataxia has raised the question of cerebellar involvement.

There may be intention tremor, suggesting a cerebellar deficit. Some have unsteadiness, lightheadedness, or dizziness. However, vertigo, nystagmus, cerebellar dysarthria, and scanning speech are usually absent.

Patients which Fisher's syndrome most often have an elevated spinal fluid protein, but they are more likely than typical GBS patients to have normal CSF. The electrophysiologic studies show mild slowing of nerve conduction velocities compared with typical GBS and are more likely to be normal in the limbs than

INVESTIGATIONS :

CSF ANALYSIS:

Within first few days, most patients develop an abnormal spinal fluid profile,with high cerebrospinal fluid protein in the absence of a pleocytosis(albuminocytologic dissociation). Glucose is normal, as are cultures. The elevation of CSF protein is presumed to result from a breakdown of the blood-CSF barrier. In the first day or two, the CSF protein is commonly normal. In Popper's series, 34% of patients had normal CSF protein in the first week, whereas in the second week only 18% were normal. Serial CSF studies

may be needed to demonstrate an abnormality. Upto 5% to 10% of GBS patients may have a lymphocytic pleocytosis, with as many as 100 WBC/cumm. In patients with CSF pleocytosis, a possibility of GBS associated with HIV infection, Lyme diseases, or sarcoidosis should be considered.

The examination of CSF typically shows normal pressure, few or no cells, and a protein concentration above 0.55g/litre after the first week of illness. A normal CSF protein level, particularly in the early illness, or a finding of numerous lymphocytes does not exclude the diagnosis, but a protein level above 2.5 mg/litre raises the suspicion of spinal cord compression and pleocytosis may signify Lyme disease, neoplasis, HIV, sarcoid meningitis or other disease.

NERVE CONDUCTION STUDIES :

Abnormalities of nerve conduction are most sensitive and specific laboratory findings in GBS. They occur earlier and more frequently than elevation of protein in the CSF.

Electromyography and nerve conduction studies can document peripheral nueorpathy that is of a demyelinating type. The characteristic findings of presence of early demylination i.e., conduction block. Demyelinating neuropathy tends to produce very slow nerve conduction velocities, dispersed compound muscle action potentials (CMAP), and

multifocal conduction block. Initially, the abnormality on nerve conduction studies may be limited to very prolonged F-waves. Conduction block in motor nerves causes the weakness in GBS, and spontaneous discharges in demyelinated sensory nerves probably cause the paresthesia and pain.

In the first few days the nerve conduction studies may be normal or only mildly abnormal. The electrophysiological abnormalities tend to lag behind the clinical examination. Severe reduction in the CMAP amplitudes may predict the long- term outcome. Miller et al showed that CMAP amplitudes less than 10% of normal were associated with a less favorable long-term prognosis. Similarly, the North American Guillain-Barre study group noted a worse prognosis associated with CMAP amplitude less than 20% of normal. However such observations are not universally accepted as Triggs found that 50% of patients with severely reduced CMAP amplitudes were clinically normal at 1 year.

Normal electrophysiological studies after several days of illness, particularly in patients with substantial weakness should direct attention away from GBS.

Alternative diagnosis are also suggested by reflexes that remain normal for more than several days in weak and paresthetic limbs, marked asymmetry in weakness, or fever in initial stages a few patients may have a band sensation

around the thorax, transient sensory levels, persistent but diminished reflexes, early urinary retention or Babinsky's signs without other signs of myelopathy, but presence of aberrant findings or diminished sensations below a trunk indicates spinal cord disease

COMPLICATIONS :

The common complications of GBS include respiratory failure, atelectasis, aspiration, pneumonia, bladder dysfunction, pain, depression, phlebitis, pulmonary embolus and syndrome of inappropriate antidiuretic hormone secretion (SIADH) exacerabated by positive pressure ventilation. Pseudotumor cerebri, papilloedema alone and unexplained seizures have been reported.

Further complications from immobility and bedrest include decubitus ulcers secondary compression neuropathy such as ulnar neuropathy and peroneal neuropathy, and the psychiatric sequelae associated with a prolonged, immobilizing stay in the ICU.

DIAGNOSIS

Early acute GBS may be difficult to identify and has no pathogomonic features, but fully evolved pattern is easily recognised.

In 1978, National Institute of Neurological and Communicative Disorders and Stroke (NINCDS, now NINDS) criteria for diagnosis of GBS were revised.

Diagnostic Criteria for classical GBS

A. Features required for diagnosis :

1. Progressive motor weakness of more than 1 limb.

2. Areflexia.

B. Features strongly supporting the diagnosis :

i. Clinical features:

1. Progression of symptoms and signs over days upto 4 weeks.

2. Relative symmetry of symptoms.

3. Mild sensory symptoms or signs.

4. Cranial nerve involvement, especially facial diplegia.

5. Recovery beginning 2-4 weeks after the progression ceases.

6. Autonomic dysfunction.

Absence of fever at the onset of illness.

ii. . CSF picture:

1. Elevated CSF protein after 1 week of symptoms.

2. Cell counts of less than or equal to 10 mononuclear leucocytes per cumm of CSF.

iii. Electrodiagnostic studies:

1. Evidence of nerve conduction slowing or block.

C. Features making the diagnosis doubtful :

i. Marked persistent asymmetry of weakness.

ii. Marked bladder or bowel dysfunction at the onset or its persistence thereon.

iii. Presence of polymorphonuclear leucocytes or > 50 mononuclear leucocytes per cumm of CSF. iv. Sharp sensory level.

D. Features excluding the diagnosis.

1. Diagnosis of acute intermittent porphyria or recent diphtheria infection.

2. Diagnosis of botulism, poliomyelitis, hysterical paralysis, toxic neuropathy (lead, nitrofurantoin dapsone) or history of hexacarbon abuse.

3.Pure sensory syndrome

Suggestions and comments regarding modification of the above criteria were subsequently proposed by Asbury and Cornblath in 1990. These are as follows:

1. Distal areflexia with definite hyporeflexia of biceps and knee jerks will suffice if other features are consistent.

2. Fever may be present at the onset of symptoms.

3. Severe sensory loss with pain can be seen in some cases.

4. Occasionally the patient's disease will continue to progress for more than 4 weeks

5. Occasional patient may have severe ataxia, dysarthria, extensor plantar responses and ill-defined sensory levels. These need not exclude the diagnosis if other features are typical.

6. Very rarely in CSF, proteins fail to rise in the 1 to 10 weeks period after onset of symptoms and mononuclear cell counts upto 50 per cumm may be seen. The lack of albuminocytological dissociation in some patients of GBS has also been reported from India. In HIV related GBS, the cell count of upto 50 cells/cumm is considered a normal, rather than a variant.

7. upto 20% of patients may have normal conduction studies, and more over these may not become abnormal until several weeks into the illness. The yield of findings consistent with demyelinating neuropathy is increased by studying late responses (F waves and H reflexes), evaluating proximal nerve segments nd performing precise enough measurements to determine whether partial conduction block and abnormal temporal dispersion exist.

TREATMENT:

All patients with suspected GBS should be hospitalized for vigilant monitoring due to the high risk of respiratory failure and need for intubation and mechanical ventilation. Baseline spirometry, including FVC and oximetry,

should be obtained. The cornerstone of treatment is that of meticulous general medical support.

Very mild cases with only distal paresthesia and mild limb weakness may not need treatment, but it is advisable to wait approximately two weeks before concluding that there will be no further progression. Patients with vital capacities that are rapidly declining or below 18ml/kg or those with cardiovascular dysautonomia are appropriate candidates for observation in an ICU.

The most important advances in treatment of GBS have been positive pressure ventilation and intensive respiratory and medical management in the ICU, both introduced during the European Poliomyelitis Epidemic of the 1950s. These have allowed patients with complications of immobilisation and respiratory failure to survive and recover from paralysis.

The criteria advocated for intuabation, weaning and extubation in GBS are:

A. Intubation :

1. Mechanical ventilatory failure with vital capacity (VC) of 12-15 ml/kg. Falling VC over 4-6 hours or clinical signs of fatigue (brow sweating, tachycardia, hyperpnea) may prompt intubation at 15ml/kg
2. PaO2 less than 70mmHg on inspired air.

3. Severe oropharyngeal paresis with difficulty in clearing secretions or repeated coughing and aspiration after swallowing.

B. Weaning from ventilator:

1. When VC exceeds 8-10 ml/kg with adequate oxygenation maintained with 35- 40% inspired oxygen.

2. Patient can voluntarily double resting minute volume.

C. Extubation :

1. When continuous positive airway pressure of 5-7 cm of water was tolerated without clinical signs of fatigue for 12-24 hours

2. Arterial Pao2 greater than 9O mmHg on room air.

3. Adequate alveolar ventilation.

4. Improvement in bulbar paresis.

Although many patients of GBS have clinical signs of fatigue of respiratory muscles, only 10% - 30% patients eventually require mechanical ventilation. Indications for intubation include an FVC dropping below 12ml/kg or in a normal- sized adult, FVC falling below 1 liter patients who are subjectively dyspneic or appear to be struggling to breathe should be intubated, even if their FVC is above these levels. In general one should err on the side of early intubation than late. A simple bedside estimate of FVC can be made by having the patient count out loud. If the patient can take a maximal inspiration

and then can count upto 25 probably about 2 liters. A patient who can count upto 10 probably has about 1 liter FVC.

In patients with respiratory failure, the average duration of machine assisted respiration has been 50 days. In a study form India, 30% of the patients studied required mechanical ventilation.

In patients with respiratory failure, the average duration of machine assisted respiration has been 50 days. In a study form India, 30% of the patients studied required mechanical ventilation. Weakness of facial, truncal, neck, bulbar and proximal weakness of upper limb and automic disturbances were predictors for need for subsequent mechanical ventilation.

The prevention of nosocomial infections is another central feature of treatment, since 25% of patients acquire pneumonias and 30% acquire urinary infections. Prophylaxis for pulmonary embolism, adequate nutrition, and psychological care are the other major areas of concern in severe cases.

As many as 30% of patients with GBS, experience significant pain early in their presentation and may be more pronounced in the limbs. Conventional analgesics may be useful, in addition to those commonly used for treating neurogenic pain (such as tricyclic antidepressent medications). Alternatively, a brief course of high-dose corticosteroids can lead to marked improvement in pain control.

IMMUNOTHERAPY OF GBS :

Corticosteroids :

For 50 years corticosteriods were the main stay of treatment for acute GBS on the basis of anecdotal experience, a few uncontrolled studies and the appeal of their anti-inflammatory effect.

Two randomized controlled trails, one using conventional doses of prednisolone for two weeks[41] and the other, use high dose (500 mg) intravenous methylprednisolone[42] daily for 5 days have found no benefit. Steroids are thus no longer considered useful for GBS.

Plasma Exchange:

Evidence of the presence of antibodies[43] or demyelinating serum factors has provided a rationale for use of plasma exchange in therapy of GBS. In 1978, Brettel et al[44] first reported the benefits of plasma exchange in the treatment of GBS. Since then, several trials have been confirmatory.

Three large studies-North American GBS study group,[45] the French[46] and Swedish[13] trials have established benefits of plasma exchange. The conclusions derived from these three trials were: Plasma exchange is beneficial in acute GBS; It favourably modifies poor prognostic factors; Maximum benefit is obtained when it is instuited early(within first 2 weeks) In the usual regimen of plamapheresis,[21] a total of 200-250ml. / kg body

weight is removed in 4-6 cycles on alternate day The time required to complete a series of exchanges is 8 - 14 days. Plasma as replacement fluid is not recommended[46] and now a days albumin or saline is used. The type of replacement fluid (albumin / saline) used in plasma exchange has not been found to influence the outcome.

Patients undergoing plasma exchange on continuous flow machine have a better outcome than on intermittent flow machines.[33] Two continuous flow techniques can be used : Ultrafiltration and centrifugation. In a recent study, no difference was found.[47]

Indications for starting plasma exchange in patients of GBS have been advocated by Mckhann and Griffin.[48] These are: inability to walk unaided; rapid and significant reduction in serial vital capacity and onset of bulbar paralysis. The benefit of plasma exchange is diminished if treatment is begun after two weeks of illness but some patients still seem to benefit if their condition continued to worsen during third week. After an initial good response with plasma exchange, some patients may show deterioration necessitating further series of plasma exchange.

Complications of plasma exchange[49] also has certain practical limitations like: availability of technical set up and trained personnel to carry out the procedure; greater risk for patients with cardiovascular complications

or marked dysautonomia (associated with GBS) and small but real risk of transfer of infections (hepatitis and HIV) when plasma is used as replacement fluid.

Modified Plasma Exchange: A study from India[50] showed that small volume plasma exchange (10 -15ml/kg of plasma exchanged on consecutive days) during first two weeks of the illness showed results comparable to that of conventional plasma exchange (200 -250 ml/kg). A similar study report from Sri Lanka[61] has supported this fact. All this was achieved at a lower cost and fewer complications which is important for widespread application in developing countries. The replacement fluid used in these studies was fresh frozen plasma.

Immunoglobulins:

High dose intravenous immunoglobulin was first reported to be beneficial in GBS by Kleywey et al[52] in 1988.

Intravenous immunoglobulin has been found to be useful in treatment of many diseases with an autoimmune basis. The proposed mechanisms[53] for their action

a. Passive transfer of neutralizing anti-idiotypic antibodies against auto antibodies.

b. Intravenous immunoglobulin alters the structure and dynamics of the idiotypic network in the auto immune patient to regain physiological control of auto immunity.

During the first week of illness, the preferred treatment for patients with GBS who have severe disease and require assistance to walk is either plasmapheresis or intravenous immunoglobulin. A controlled, randomized trial[47] comparing intravenous immunoglobulin treatment with plasma exchange concluded that intravenous immunoglobulin was also effective as first line treatment. In this study, 52.7% of 74 patients receiving immunoglobulin compared with 34% of 73 patients undergoing plasma exchange had functional improvement of one grade or more after 4 weeks. Although immunoglobulin was clearly more efficacious, this findings was challenged because response to plasma exchange in this study[47] was inferior to that in earlier studies.[45] This prompted a new multinational, multicentre trial[54] that compared efficacy of immunoglobulin alone, plasmapheresis alone and plasmapheresis followed by immunoglobulin. After 4 weeks of treatment and 48 weeks of follow up, no statistically significant difference was seen between the treatments.

Consequently the question of which therapy is preferable for using first considering their similar efficacy and cost is a matter of convenience and practicality.[55]

The indications for immunoglobulin in GBS have not been clearly laid down yet. In the Dutch study trial,[47] inclusion criteria included acute GBS, inability to walk 10metres independently and presentation within 2 weeks of disease onset. If the illness continues to worsen in the first 15 days despite a full course of plasma exchange, a trial of immunoglobulin therapy[55] is warranted. The dose recommended is 0.4g/kg/day for 5 days. Just like plasma exchange, the use of immunoglobulin has also been associated with treatment related fluctuations.

Adverse reactions[55] to immunoglobulin therapy are usually minor and occur in about 10% of patients. Side effects include fever, myalgia, headache, meningism, and eczema on hands. There is also an increased risk of thromboembolic events, as therapy with immunoglobulin increases serum viscosity. Anaphylaxis is very rare but potentially fatal. Immunoglobulin should be used with extreme caution in patients with renal failure which it may exacerbate.

REHABILITATION:

Rehabilitation requires an organised program with definite end points. There are no systematic studies of physiotherapy in GBS. But early goals include, preventions of decubitus ulcers, tendon shortening, joint malalignment, peroneal nerve compression palsies and facilitation of

pulmonary toilet. Psychological problems in form of depression, mental fatigue, impotence and those due to residual weakness should also be tackled.

OUTCOME:

Although GBS is often thought to have a benign prognosis, 7% of patients die and a further 16% suffer significant residual disability.[66]

Speed of recovery varies and may take 6-8 months; no improvement is expected after 2 years.[57] Remyelination is usually complete but recovery is poor when there has been Wallerian axonal degeneration[58] after which the axons regrow at 1mm per day - so many do not reach their target muscles for several years if at all.

The death rate has varied from 1.3% in different series with a mean of 6%, probably depending more on the quality of intensive care than specific treatments. Half of the deaths[58] are within first month - one third from cardiovascular autonomic complications such as asystole; a quarter from pneumonia or respiratory failure and the rest from pulmonary embolism, infection, infarction, renal failure and unrelated cause.

With the currently available modalities of treatment, it is estimated that about 15% of GBS patients completely recover without any deficit and another 65% have persistent minor problems that generally do not impair conduct of everyday life.[21] The disease in itself does not result in chronic fatigue but mild

depression indicated by persistent mental fatigue is common. A few men have residual impotence. Three percent of patients may have one or more recurrence[57] of the disease.

PROGNOSIS

Although the majority of patients with GBS make an acceptable functional recovery,a proportion succumb to the acute illness while others retain significant residual disability. It is thus important to be able to select only patients with a poor prognosis for treatment, which often involves discomfort, expense and risk others retain significant residual disability. It is thus important to be able to select only patients with a poor prognosis for treatment, which often involves discomfort, expense and risk of complications.

No large-scale prospective study has ever been carried out and the available retrospective studies give an incomplete picture of outcome. It is also difficult to estimate how many patients remain disabled from literature. Hence a number of small studies have been conducted to correlate particular clinical features with a poor outcome

Osier and Sidell[59] suggested that patients with a strictly motor neuropathy and no sphincter disturbances were more likely to have a benign prognosis. However Marshall[60] described 37 patients including some with

severe sensory loss or sphincter disturbance and could find no evidence that such features influenced outcome adversely.

A particularly severe motor deficit appears to carry a greater risk of residual disability according to a number of authors.[61] Two paediatric studies [61,62] have suggested that the time taken to improve also has prognostic value. They concluded that an interval of greater than 18 days from maximum deficit to onset of improvement (plateau) was associated with incomplete recovery. Other factors common in the poor outcome group were absence of tendon reflexes from onset, severe weakness in distal muscles and a relatively low CSF protein. However majority of studies have failed to find any correlation between CSF protein and outcome.

In a study by J.B. Winer et al,[61] time taken to become bed bound, severity of peak deficit, need for assisted ventilation, age greater than 40, and small compound muscle action potentials in the abductor pollicis brevis elicited by stimulating the median nerve, were found to be associated with poor outcome. However, time from onset of weakness until improvement began and duration of plateau phase, failed to show a significant correlation with outcome. This conclusion conflicts with previous observations[56] in which failure to improve within 3 weeks of reaching peak deficit adversely affected outcome. In yet another study by NK Singh et al,[53] rapid progression of illness, severe degree of paralysis and muscle wasting, prolonged period of peak

paralysis lasting more than weeks, delayed onset of recovery not commencing within 3 weeks from onset of weakness, bulbar paralysis and respiratory involvement adversely affected outcome. Evidence of axonal damage in electrodiagnostic studies was also associated with poor outcome. However age, sex, severity of sensory loss, sphincter disturbances, CSF findings and nerve conduction velocity did not significantly affect outcome. Autonomic dysfunctions were noticed in 66.6% cases but were mostly mild and transient, and did not affect longterm outcome.

MATERIALS AND METHODS

All adult patients (> 12 years of age) diagnosed as Guillain Barre Syndrome (GBS) fulfilling the criteria as modified by Asbury, admitted in the medical wards of Rajiv Gandhi Govt. General Hospital, Chennai-3, from April 2013 to March 2014 were included in this study.

A detailed history with particular attention to the date of onset of neuropathic signs and the tempo of ensuing functional disability was elicited and a clinical examination was performed at admission as per the proforma.

Repeat examinations of muscle power were performed on alternate days till discharge and follow up examination at the end of 3 months. Autonomic function tests were performed at admission and repeated at peak disability. During each examination, the following were noted:

1. Medical Research Council Grading of muscle weakness.
2. Disability Grade (0 - 6) was noted according to the following.

   0 - Healthy.

   1 - Minor symptoms or sings.

   2 - Able to walk 5m without assistance, walking frame, or stick but unable to do manual work including housework, shopping or gardening.

   3 - Able to walk 5m with assistance, walking frame, or stick.

4 - Chair/bedbound.

5 - Requiring assisted ventilation (for at least part of day or night).

6 - Dead.

3. Bedside Autonomic function tests - Resting Heart rate, Resting Blood Pressure, Postural Hypotension, Blood pressure changes at the end of one minute and 3 minutes on standing from lying position, wherever possible. In addition complaints suggestive of autonomic dysfunction such as excessive sweating, urinary retention and constipation, palpitations, postural giddiness were also noted.

Criteria for autonomic dysfunction:

Tachycardia : Resting heart rate above 100 beats per minute in the absence of any secondary cause for increased heart rate such as fever or hypoxia.

Bradycardia: Resting heart rate below 60 beats per minute.

Hypertention: Supine/sitting blood pressure of more than 140/90 mmHg in previously nomotensive patients.

Hypotension: - Systolic blood pressure less than 90mmHg.

Postural Hypotension:- Fall in systolic blood pressure by greater than 30 mmHg on standing from lying position.

Laboratory investigations were performed (as mentioned in the proforma) at admission, including hepatitis B serology and HIV serology, wherever required, Cerebrospinal fluid examination was done in all the patients and Nerve conduction studies were also done in all patients.

All patients were treated conservatively with physiotherapy and mechanical ventilatory assistance, where required. Patients who detoriotated in hospital were treated with intravenous Immunoglobulin (0.4g/kg/for 5 days) and some patients treated with steroids i.e., intravenous methylprednisolone and plasmapheresis depending on availability of drug. Time taken to reach peak deficit, interval from maximum deficit to onset of improvement (plateau time), duration of ventilatory support required and nature of complications were noted.

For analysis, patients were then divided into two groups; Disability grades 0 -3 at the end of 3 months were grouped as 'Good Outcome' whereas disability grades 4-6 were taken as 'Bad Outcome'. Frequency of various possible prognostic factors within the two groups was then determined and possible associations were tested. Statistical methods used to analyze the results included Mean + standard error of mean (SEM) value, and Fisher's exact probability test (by computer analysis). P values of <0.05 were considered significant.

RESULTS & OBSERVATIONS

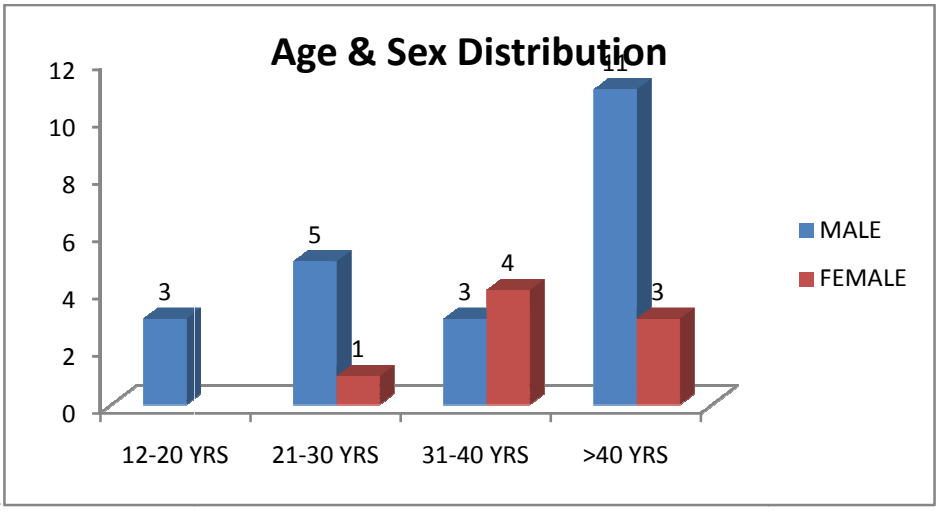
A total of 30 patients were studied. All patients were hospitalised and the average duration of hospital stay was 17.57 days.

1. Age and Sex distribution:

Twenty-two patients (73.33%) were males and 8(26.67%) were females. The age of patients ranged from 13 to 67 years (Mean age 40.87 years) with the maximum number (46.67%) of patients in the above 40 age group (Table-1).

Table 1: Age and sex distribution

Sex	Age				Total
	12 - 20	21-30	31-40	>40	
M	3 (10%)	5 (16.67%)	3 (10%)	11 (36.67%)	22 (73.33%)
F	-	1 (3.33%)	4 (13.33%)	3 (10%)	8 (26.67%)
Total	3 (10%)	6 (20%)	7 (23.33%)	14 (46.67%)	30 100%)



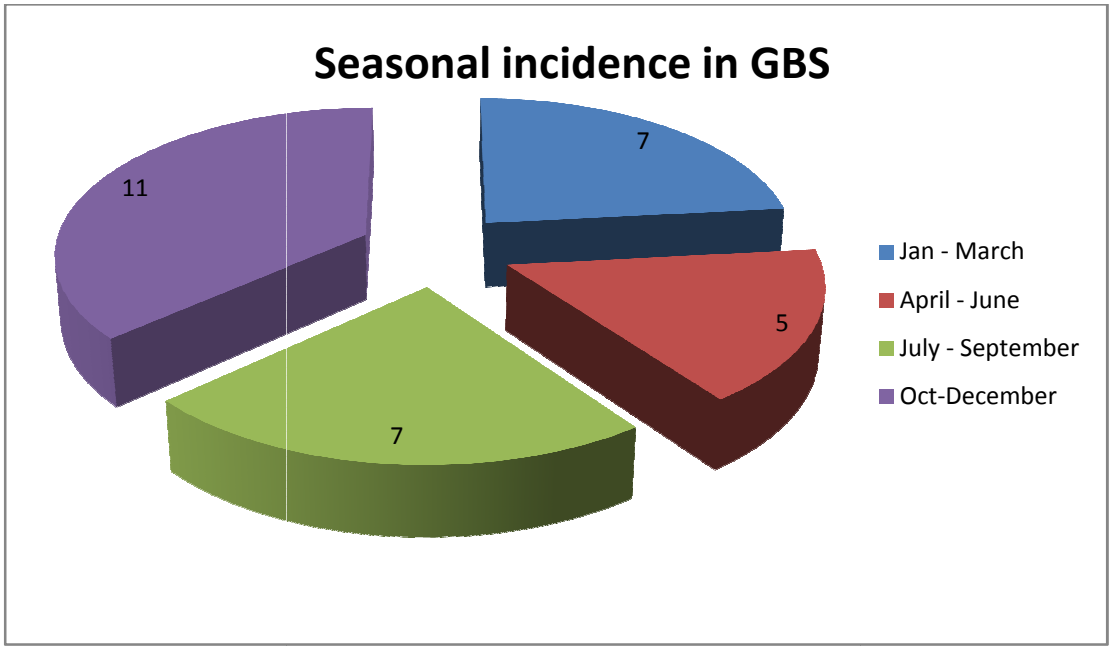
2. Seasonal incidence :

The least number of cases were seen in the months of April to June.

However no significant increased incidence in any particular season could be inferred. (Tablc-2).

Table 2 : Seasonal incidence in GBS

Months	No. of cases	Percentage
Jan - March	7	23.36%
April - June	5	16.67%
July - September	7	23.36%
Oct-December	11	36.67%

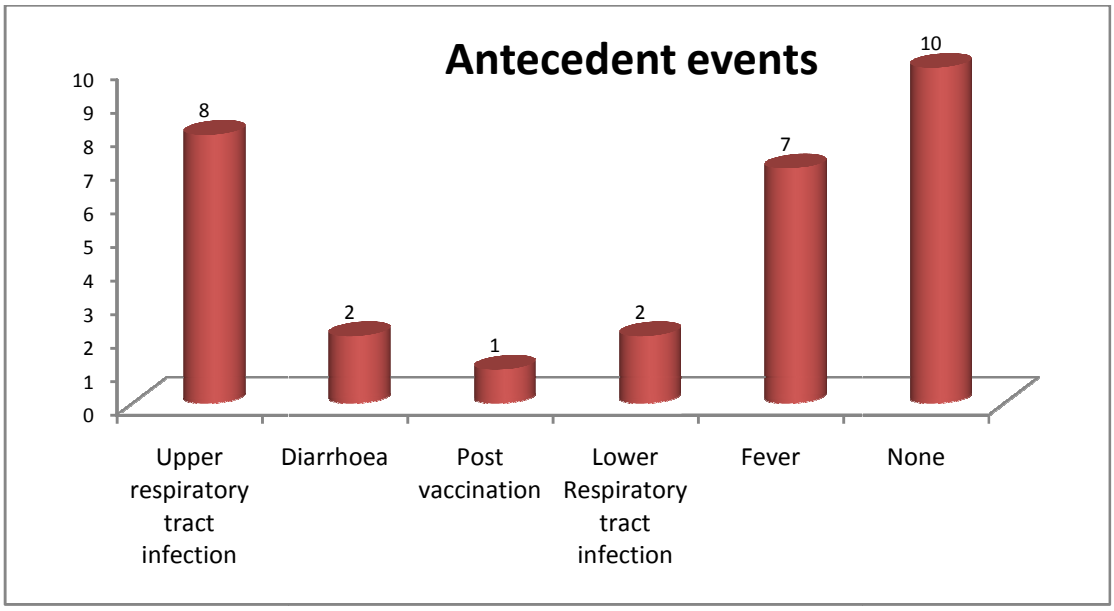


3. Preceding illness:

Twenty (66.67%) patients had some antecedent event prior to the development of GBS (Table-3). The most common antecedent illness was upper respiratory tract infection. In patients with a history of preceding illness, the mean duration between onset of GBS and the preceding illness was 9.06 (± 4.21) days.

Table 3 : Antecedent events

Antecedent events	No. of patients	Percentage (%)
Upper respiratory tract infection	8	26.67
Diarrhoea	2	6.67
Post vaccination	1	3.33
Lower Respiratory tract infection	2	6.67
Fever	7	23.33
None	10	33.33



4. First Symptom of illness:

The first symptom of the illness was in the form of motor weakness in 11 (36.67%) patients and it was sensory in the form of pain, paraesthesiae or numbness in the remaining 19(63.33%) patients. Details are shown in Table-4.

Table 4. First symptom

Motor symptoms	**No. of patients**	**Percentage**
Weakness of legs	6	20
Weakness of legs and arms	2	6.67
Weakness of arms alone	3	10
Total	11	36.67
Sensory symptoms	**No. of patients**	**Percentage**
Paraesthesiac	10	33.33
Pain in legs	3	10
Pain in back	2	6.67
Numbness in legs	2	6.67
Generalised muscle aches	2	6.67
Total	19	63.33

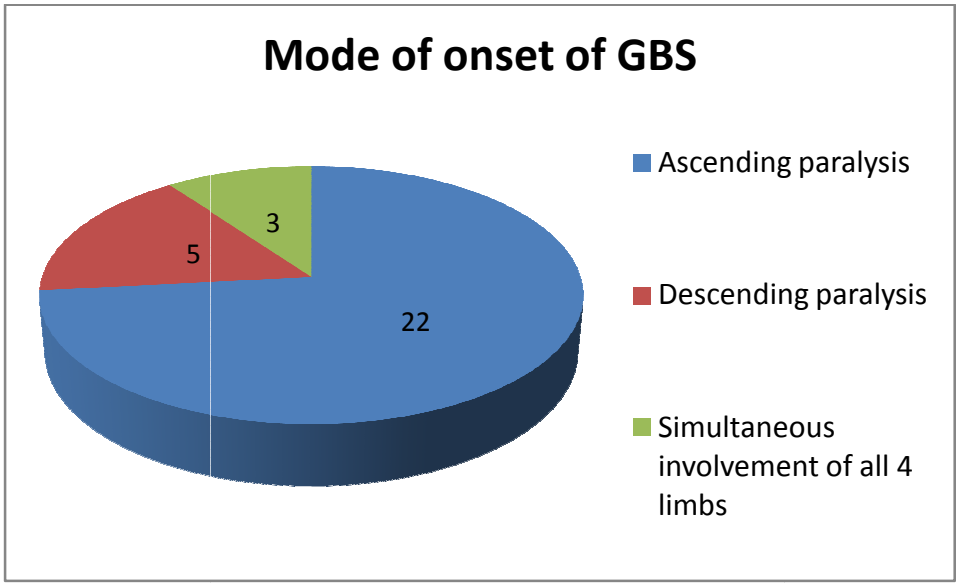
Twenty two (73.33%) patients experienced some sensory symptoms during the course of their illness mainly in the form of paraesthesiae in hands and feet. Eight (26.67%) patients did not have any sensory symptoms throughout the course of their illness.

5. Mode of onset:

Twenty two patients (73.33%) had ascending form of paralysis. Only 5 (16.67%) patients had descending type of paralysis (Table-5). Muscle weakness occurred in the proximal muscles initially and later progressed to the distal muscles in 17 patients. Progression from distal to proximal muscles were seen in 9 patients, three patients had simultaneous involvement of both proximal and distal muscles.

Table 5. Mode of onset of GBS

Mode	No. of patients	Percentage
Ascending paralysis	22	73.33%
Descending paralysis	5	16.67
Simultaneous involvement of all 4 limbs	3	10%



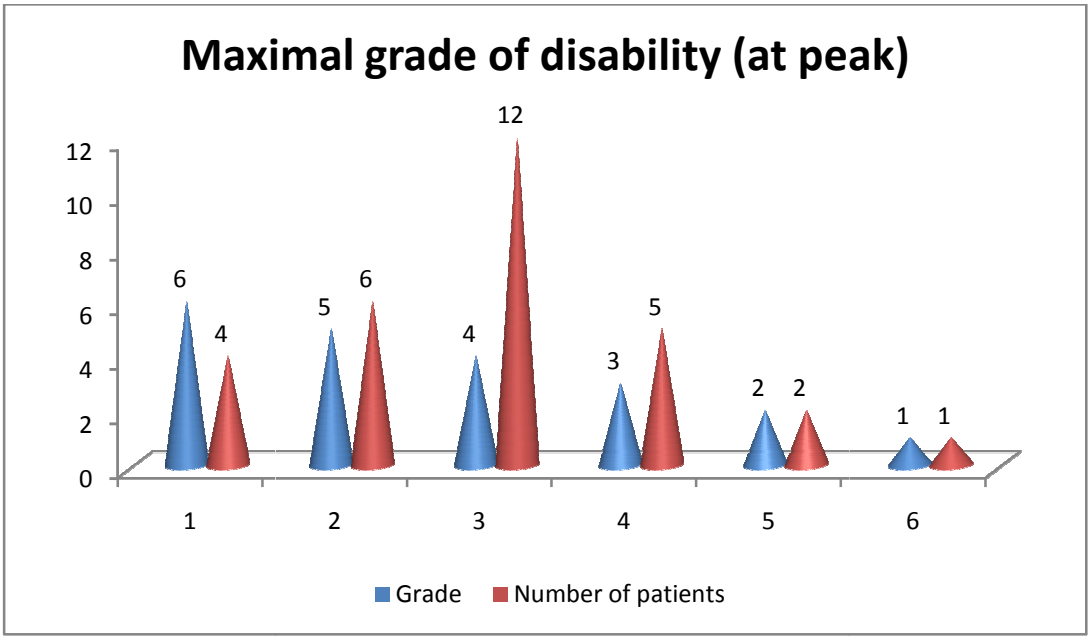
6. Maximal grades of disability:

Twelve patients took upto 1 weak to reach maximal weakness, 15 patients took upto 2 weeks, 2 patients took upto 3 weeks and 1 patient took longer than 3 weeks (24 days). The maximum number of admitted patients (40%) reached grade 4 disabilities at peak (Table-6).

Ten patients (33.33%) developed respiratory paralysis and required mechanical ventilation. Four (13.33%) patients died. The cause of death was septicaemic shock following aspiration pneumonia in 1 patient and cardiac arrest while on mechanical ventilation in other 3 patients. One of the patients, who had a cardiac arrest, had severe autonomic dysfunction with fluctuating blood pressure and heart rate.

Table 6. Maximal grade of disability (at peak)

Grade	Number of patients	Percentage
6	4	13.33%
5	6	20%
4	12	40%
3	5	16.67%
2	2	6.67%
1	1	3.33%



7. Sensory Deficit:

Objective sensory loss was elicited in only 3(10%) out of the 30 patients. The sensory deficit was in the form of diminished touch, vibration and joint position sense, which occurred in a glove and stocking distribution.

8. Cranial Nerve Dysfunction:

Eighteen patients (60%) had cranial nerve dysfunction. (Table-7) Seventeen patients had facial nerve palsy, among which 15 were bilateral. Six patients had involvement of 9^{th} and 10^{th} cranial nerves. Total external ophthalmoplegia was observed in one patient. This patient also had severe ataxia and weakness in the lower limbs. A diagnosis of Miller Fisher variant of GBS was made in this patient. Hypoglossal nerve was involved in one patient. One patient had left recurrent laryngeal nerve palsy.

Table 7. Cranial nerve dysfunction

Cranial Nerve	Number of patients	Percentage
VII -Unilateral	2	6.67%
Bilateral	15	50%
IX, X	6	20%
III, IV, VI	1	3.33%
XI	1	3.33%
XII	1	3.33%

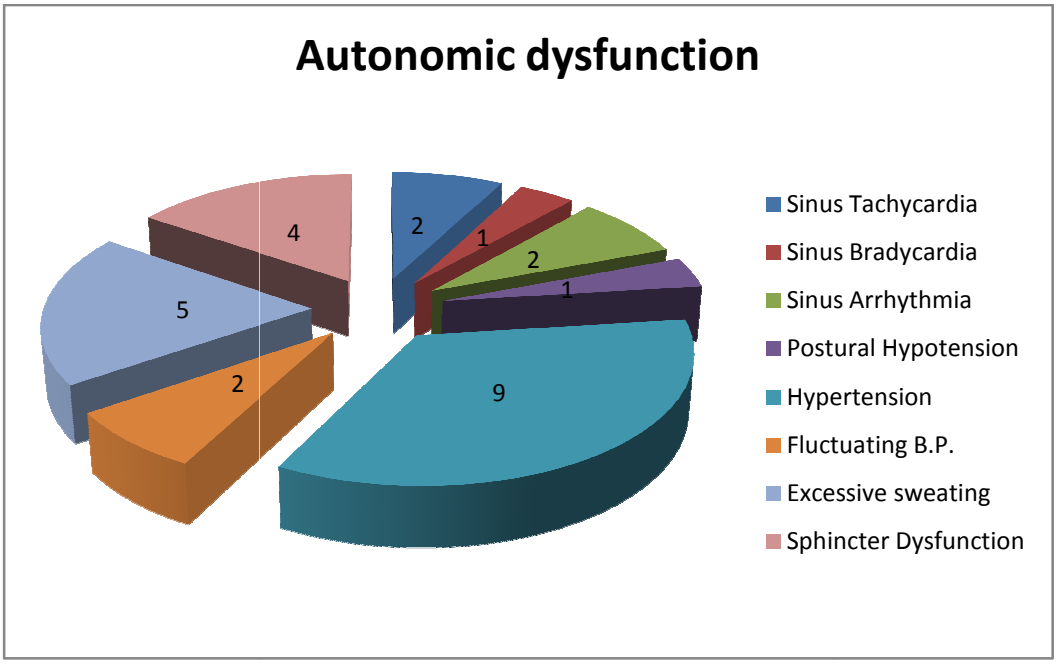
9. Autonomic dysfunction:

Patients who were in Grade 4 disability or more were not subjected to standing blood pressure recordings. Only sitting blood pressures were recorded in these patients. In patients who were on ventilator, the spontaneous changes in heart rate and blood pressure were noted.

Autonomic dysfunction was detected in 14 (46.67%) patients Table-9.

Table 8. Autonomic dysfunction

	Number of patients	Percentage
Sinus Tachycardia	2	6.67%
Sinus Bradycardia	1	3.33%
Sinus Arrhythmia	2	6.67%
Postural Hypotension	1	3.33%
Hypertension	9	30%
Fluctuating B.P.	2	6.67
Excessive sweating	5	16.67%
Sphincter Dysfunction	4	13.33%



10. Cerebrospinal Fluid (CSF) Analysis:

CSF pressure was normal and CSF was clear in all patients. CSF glucose was also normal (approximately half the blood glucose level) in all patients.

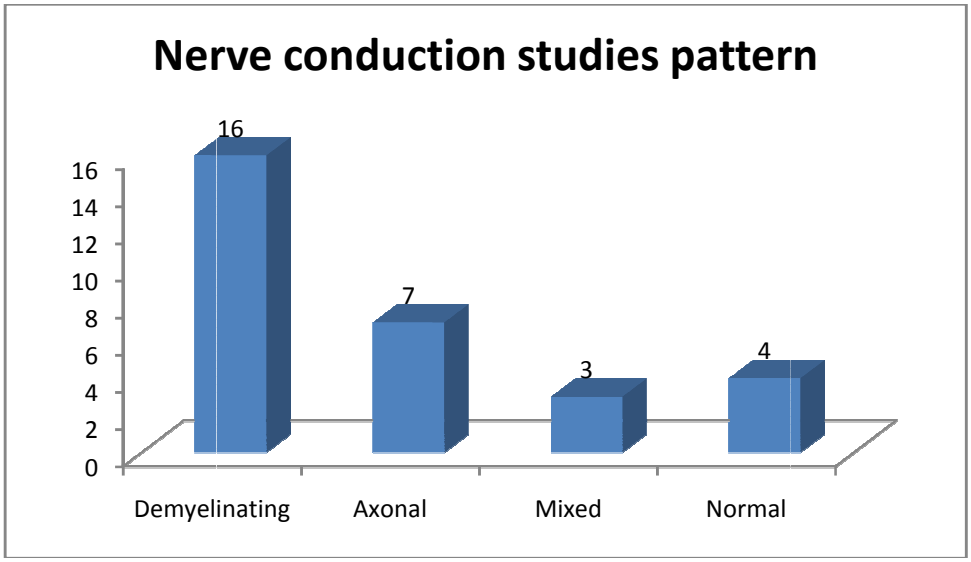
CSF protein concentration was raised above 50 mg% in 20 (66.67%) patients at one week. Three patients had lymphocytic pleocytosis of 20, 30 and 50 cells/cumm. None of the remaining patients had CSF pleocytosis.

11. Electrophysiological studies:

Nerve conduction studies were conducted in all patients. Sixteen patients were found to have reduced motor conduction velocities consistent with demyelinating neuropathy. Seven patients were found to have decreased amplitude of action potentials consistent with axonal pattern of neuropathy. Three patients had mixed pattern of neuropathy. The remaining 4 patients had normal conduction studies.

Table 9. Nerve conduction studies pattern

Type	Number of patients	Percentage
Demyelinating	16	53.33%
Axonal	7	23.33%
Mixed	3	10%
Normal	4	13.33%

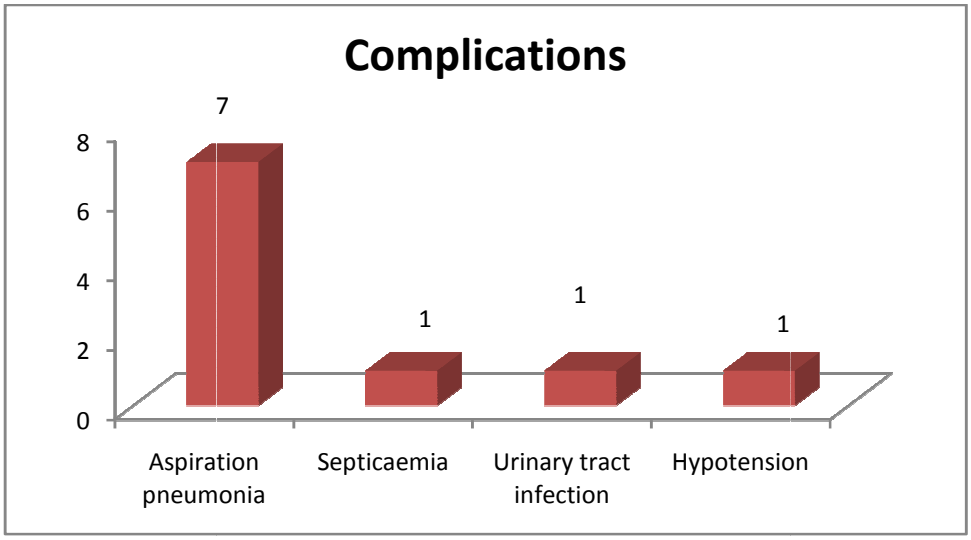


12. Complications:

Complications observed are listed in Table-10.

Table 10. Complications

	Number of patients	Percentage
Aspiration pneumonia	7	23.33%
Septicaemia	1	3.33%
Urinary tract infection	1	3.33%
Hypotension	1	3.33%



13. Treatment:

All patients received physiotherapy and the 10 patients who developed respiratory failure were put on mechanical ventilation. Two patients received intravenous immunoglobulins in addition to conservative therapy. Both of them showed good response with arrest of progression of muscular muscle weakness by 2 to 3 days. 3 patients received intravenous methylprednisolone. Patients with intravenous steroids did not show much benefit over supportive treatment. 3 patients received plasmapheresis. Among them 2 patients responded well with arrest of progression of muscle weakness and one patient expired on ventilator.

14. Mortality:

Four patients (13.33%) died in this study. All four patients developed respiratory failure and required assisted mechanical ventilation. One patient developed aspiration pneumonia and later died due to septicaemia and shock. The other 3 patients died while on ventilation due to cardiac arrest. In one of these patients, severe autonomic dysfunction was observed. The patient had fluctuating blood pressure and sinus tachycardia followed by sinus bradycardia unresponsive to atropine. He finally died due to cardiac arrest. The cause of cardiac arrest in the other two was unexplained.

15. Analysis of prognostic factors:

Twenty-five out of 30 patients were analysed for prognostic factors in GBS at the end of 3 months. The rest 5 patients were lost to follow up.

Patients were divided into two groups. A 'Good Outcome' group which had a disability grade of 3 or less at the end of 3 months and a 'Poor Outcome' group which had a disability grade of greater than 3 at end of 3 months. Eighteen (72%) patients were found to have a good outcome while 7 (28%) had a poor outcome.

FEATURES OF GOOD AND POOR OUTCOME GROUPS:

Table 11. Features of good and poor outcome groups

Features	Good Outcome	Bad Outcome
Mean time to peak (days)	10.7 (±3.24)	7.29(±2.16)
Median time to onset of improvement	14 days	22 days
Median plateau time (days)	4 days	10 days
Median C.S.F. protein	61 mg%	63 mg%

Patients were then analysed using Fisher's Exact Probability Test with reference to various prognostic factors and their significance determined.

PROGNOSTIC NEUROGLOGICAL SIGNS

1. AGE:

Patients were grouped into two categories: a) 40 years and below and b) above 40 years of age.

Outcome was then determined in each of these groups and the significance of age above 40 years as a poor prognostic sign was determined (Table-12).

Table 12. Age in relation to outcome

Age	Number of patients	Good outcome number (%)	Bad outcome number (%)	p. value
<=40	15	11 (73.33%)	4 (26.67%)	0.2151
>40	10	7 (70%)	3 (30%)	

The above table shows that age is not a significant factor in prognosis.

2. CRITICAL TIME PERIODS

Table 13. Critical time periods in relation to outcome

(at 3 months following)

Critical time period	Number of patients	Good outcome number (%)	Bad outcome number (%)	p.value (Fisher's test)
Onset of peak paralysis				
Upto 1 week	7	3 (42.86%)	4(57.14%)	0.042
> 1 week	18	15 (83.33%)	3 (16.67%)	
Peak paralysis period (Plateau)				
Upto 1 week	17	15 (82.24%)	2(11.76%)	0.0016
> 1 week	8	3	5 (62.5%)	
Onset of recovery				
Upto 3 weeks	20	16(80%)	4 (0%)	0.113
> 3 weeks	5	2 (40%)	3 (60%)	

Outcome was determined with reference to:

a) Time taken from onset of GBS to peak deficit:- The outcome in patients who attained peak paralysis in 1 week was compared with those who attained peak paralysis after 1 week.

Seven patients had peak paralysis within the first week and the remaining 18 patients attained peak paralysis only after 1 week. Fifteen patients in the delayed peak deficit group and 3 patients in the early peak deficit group had a good outcome. Four patients in the former group and 3 patients in the latter had a poor outcome.

The difference in outcome between these two groups is statistically significant. (p=0.042).

b) Duration of Plateau Phase:- Outcome in patients with a peak paralysis period (Plateau phase) of 1 week or less, was compared with outcome in those with a peak paralysis period of more than 1 week. Seventeen patients had a peak paralysis period of upto 1 week, while the remaining 8 patients had a plateau phase of more than 1 week. Fifteen patients in the former group and 3 in the latter group, had a good outcome. Only 2 patients in the former group had a poor outcome, whereas 5 patients in the latter group had a poor outcome. The difference in outcome at 3 months in these two groups is highly significant (p = 0.0016).

c) Duration from onset of GBS to recovery:- The outcome of patients with duration from the onset of GBS to onset of recovery of upto 3 weeks was compared with outcome of those who took more than 3 weeks to recover. Twenty patients started recovering within 3 weeks of onset while 5 patients took longer than 3 weeks. Sixteen patients in the former group and 2 in the later group had a good outcome. Four patients in the former and 3 in the later group had a poor outcome. The difference in outcome in the two groups is not statistically significant. (p=0.002) (Table-14).

Table 14. Need for ventilation

	Number of patients	**Good outcome number (%)**	**Bad outcome number (%)**	**p. value**
Present	6	1	5	0.002
Absent	19	17	2	

4. OTHERS:

Other possible prognostic factors were analysed similarly as shown in the Table-15.

Table 15. Other possible prognostic neurological signs

Neurological sign	Number of patients	Good outcome number (%)	Bad outcome number (%)	p. value
Severity of paralysis				
Power grade 0 - 1	7	2 (28.6)	5(71.4)	0.002
Power grade 2 - 4	18	16(88.9)	2(11.1)	
Sensory loss (Obj.)				
Present	3	3(100)	- (0)	0.354
Absent	22	15(68.1)	7(31.9)	
Sphincter dysfunction				
Present	4	2(50)	2(50)	0.3065
Absent	21	16(76.2)	5 (23.8)	
Bulbar paralysis				0.1937
Present	6	3(50)	3(50)	
Absent	20	16(80)	4(20)	
Autonomic dysfunction				
Present	13	8(61.5)	5 (38.5)	0.2231
Absent	12	10(83.3)	2(16.7)	

The outcome at the end of 3 months was correlated with the severity of paralysis (MRC grading) at plateau period. Seven patients had the power of 0 - 1, among whom 2 patients had a good outcome and 5 had a poor outcome. Eighteen patients had power of grade 2-4, among whom 16 had good outcome and 2 had a poor outcome. On applying Fisher's test, the difference in outcome in the two groups is found to significant regarding the severity of paralysis and final outcome (p=0.006).

The presence or absence of objective sensory loss was also compared with respect to outcome. All 3 patients who had sensory loss had good outcome. Among the remaining 22 patients with no sensory loss, 15 had a good outcome and 7 had poor outcome. The difference is not statistically significant.

Among the 4 patients who had sphincter dysfunction, equal number had good outcome and poor outcome. In the remaining patients without the evidence of sphincter dysfunction, 16 had a good outcome and 5 had a poor outcome. No statistical significance is observed in outcome between the two groups.

In 6 patients with evidence of bulbar paralysis, 3 each had a good outcome and poor outcome. In patients without bulbar paralysis, 15 and 4 patients had a good and poor outcome respectively. The difference however is not statistically significant.

Evidence of autonomic dysfunction was seen in 13 patients and 8 of them had a favourable outcome at 3 months. In paticntswithout any autonomic dysfunction. 10 out of 12 had a good outcome. The difference is not statistically significant.

DISCUSSION

A total of 30 patients were included in this prospective study. The maximum number of patients were in above 40 years age group (40%). Kaplan ct al[16] reviewed 2575 cases and found the peak incidence to be between 50 and 74 years of age with lesser peak between 15 and 35 years. Similarly Peter C. Dowling[65] also reported two peaks. In Thakaran et al[50] series however, the mean age of study group was only 28 years.

There is a male preponderance in our study which is in conformity with the report by Robert M. et al.[66] However, Peter C. Dowling's [5] study of 176 patients showed an equal incidence in males and females.

No seasonal variation in incidence of GBS could be inferred from this study in conformity with the majority of studies in literature[66]. However a few studies have noted a seasonal clustering of cases. Kaur et al[67] reported an increased incidence in summer and autumn. Peter C. Dowling[65] also noted an increase in summer.

Twenty (66.7%) of our patients had a definite antecedent event prior to onset of illness. Winer et al[61] reported that over half of GBS patients experience symptoms of viral respiratory or gastrointestinal infections. Ropper et al1 also reported a high incidence of 73%. In contrast a study by Kaur et al[67] showed a lower incidence of 32%.

The interval between prodromal illness and onset of GBS is most frequently from 1-3 weeks. Occasionally it is as long as 6 weeks. Kaur ct al[67] reported a mean interval of 9.2 days. In our study there is a mean interval of 9.06 (± 4.21) days between the prodrome and the onset of GBS. The most common antecedent illness was upper respiratory tract infection (26.67%) while diarrhoeal illness was seen in only two patients (6.67%).

Ascending paralysis was noted in 73.32 (22 patients) and descending paralysis in 16.67% (5 patients), while 10%(3 patients) had simultaneous involvement of all four limbs. According to description by Winer et al61 that muscle weakness usually starts in legs and ascends to arms in most cases. A metaanalysis of large series by Allan H. Ropper[21] showed ascending paralysis in 60%, descending paralysis in 20% and involvement of all four limbs simultaneously in 20% cases.

In 63.33%) patients, the first symptom of illness was sensory in the form of paraesthesia in hands and feet, numbness or pain whereas motor weakness was the first symptom in 36.67% of patients. However Robert et al reported first symptom as sensory in 83% and motor in 17% of patients.

73.33% of patients experienced some sensory symptoms mainly in the form of paraesthesia during the course of illness. Allan H. Ropper[21] in his metaanalysis reported 85% incidence of paraesthesia. In a study by Winer et

al[61] 75% patients had paraesthesia, Robert M, et al described 83% incidence in paraesthesia.

Objective sensory loss occurred in 3 patients (10%) in the form of diminished touch, vibration and joint position sense which occurred in glove and stocking distribution. This is much lower than the 40% reported by Allan H. Ropper[21] in his metaanalysis. Winer et al[61] noted sensory loss in 52% of his patients.

All patients had involvement of the legs and involvement of limbs was symmetric in all cases. None of the patients had involvement of hands alone, which is in conformity to the observation of Winer et al[61] who said that the arms are not affected in isolation.

One patient also had ataxia and involvement of 3rd, 4th and 6th cranial nerves. He was diagnosed to have Miller Fisher Variant of GBS.

Respiratory failure was present in 33.33% of our patients. Allan H.Ropper[21] in his meta analysis showed that 10% of patients have respiratory failure. Winer et al[61] noted a 23% incidence of respiratory failure. The average duration of mechanical ventilation in our patients was 16.12 days.

Twenty two (73.33%) patients reached grade IV or more disability (bedridden state). In the study by Winer et al[61] only 12% retained the ability to

walk throughout the illness and the remaining 88% became bedridden. This is in contrast to the report by RDM Hadden et al[58] who said 40% patients become bedbound.

Overall, about 50% of patients with GBS reach maximal weakness by 1 week, 70% by 2 weeks, and 80% by 3 weeks in the course of illness. In this study 40% of patients reached peak deficit within 1 week of onset of illness, 90% by 2 weeks.

60% of our patients had cranial nerve dysfunction. This is in conformity with the 50% incidence reported by Winer et al[61] and 60% in Allan H. Ropper's[21] meta analysis. Kaur et al[67] reported an incidence of 41% in her study from North India. Facial Nerve was the most commonly involved (56.67%) in our series in concordance with most series. IX and X cranial nerves were involved in only 20% of patients in contrast to the reported incidence of 50% in Allan H. Ropper's meta analysis.

Autonomic dysfunction is reported to occur in upto 50% of GBS patients P. Hacheneeker et al noted dysfunction in 69% of their patients. NK Singh et al[63] documented 67% incidence. In this study autonomic dysfunction occurred in 46.67% of patients.8 Transient sphineteric dysfunction in the form of urinary retention and hesitancy was seen in four (13.33%) patients. Allan H.Ropper's meta analysis reported 15% incidence of transient bladder

disturbances in GBS patients NK Singh et al[63] observed sphincter disturbance in 20% of patients.

CSF protein was raised above 50mg% in 20 patients. Winer et al[61] reported raised CSF protein in 80% patients while 90% was reported in Allan H.Ropper's[21] meta analysis. The lower number of patients with raised CSF protein in this study was probably because all CSF studies were done between 1 and 2 weeks from onset and not repeated thereafter. It is possible that there may have been a rise in CSF protein later in the course of illness, which was not recorded. Furthermore, it has been noted in some studies that CSF protein may not rise throughout the course of illness in some patients with GBS. Gupta RC[3] reports such patients did not show rise in CSF protein even at 6 weeks.

CSF pleocytosis was seen in three patients. CSF mononuclear cell counts of upto 50 per emm may be seen in GBS and does not rule out diagnosis of GBS.

Electrophysiological studies were conducted in all patients and 16 of them showed demyelinating pattern, 7 of them showed axonal pattern, 3 patients mixed pattern remaining 4 patients had normal pattern of nerve conduction studies and patients having mixed and axonal pattern showed poor prognosis compared to patients having demyelinating and normal nerve conduction study.

Many authors have found a proportion of patients to have normal nerve condution. The population varies form 9% to 20%[70] and is higher in the first few weeks of illness. This finding has been explained as due to 1) The patchy nature of pathology of GBS which means that studies confined to one or two nerves may miss abnormal findings. 2) Maximum conduction velocities may conceal abnormalities since conduction can occur normally in some fibres while being partially blocked in some others. 3) Lastly it is likely that proximal conduction blocks occur commonly in GBS that distal motor conduction would be unaffected.

Four patients died in this study. All 4 patients developed respiratory failure and required assisted mechanical ventilation. One patient developed aspiration pneunomia and later died due to Septicaemia and shock. The other 3 patients died while on ventilator due to cardiac arrest.

Case fatality in this study was 13.33%. Mortality in GBS varies from 1.3% to 13% in different series with a mean of about 6% Winer et al [1] reported 13% mortality in his study of 100 patients. NK Singh et al[63] noted 8% mortality.

PROGNOSIS:

A number of studies have been conducted in an attempt to correlate particular clinical features of GBS with prognosis in order to be able to select

only patients with a poor prognosis for a treatment which involves discomfort, expense and risk of complications.

In this study, we analysed 25 patients in relation to outcome at the end of 3 months. Patients were divided into 'Good outcome' group and 'Poor outcome' group depending on their disability grade at the end of three months. A disability grade of 3 or less at the end of three months was taken as good outcome while a disability grade of greater than 3 was considered poor outcome. Various possible prognostic factors were then analysed statistically using Fisher's exact probability test.

In a study by J.B. Winer et al[61] age greater than 40 years was found to be a significant prognostic factor. However, in a previous study by same author, age had not been found to significantly influence outcome. Similarly NK Singh et al[63] also found that age did not affect outcome. In our study too, age was not found to be a significant prognostic factor.

A poor prognosis has been observed in some studies, in patients having a rapid progression of weakness, a prolonged period of peak paralysis (Plateau) and a delayed onset of recovery, not commencing within 3 weeks from onset of weakness. Winer et al, in a retrospective study of 71 patients, noted that a prolonged plateau time and a failure to improve within 3 weeks were associated with poor prognosis.

In another prospective study[61], it was found that patients who reached peak paralysis rapidly within seven days had a poor prognosis. This study[61] contradicted the previous study[56] in that prolonged plateau period and a delayed onset of recovery were not found to be significant factors in prognosis. The study by NK Singh et al[63] found that all three time periods i.e., rapid progression to peak paralysis within seven days, prolonged plateau period, and a delayed onset of recovery greater than 3 weeks, were significant prognostic factors. In this study rapid progression to peak paralysis within seven days and prolonged plateau period greater than 7 days were found to be significant prognostic factors. However delayed onset of recovery of more than 3 weeks was not found to be a significant prognostic factor.

Mean CSF protein level in both the good outcome and the poor outcome groups did not show marked difference indicating that CSF protein concentration does not influence the outcome n these patients. This is in accord with majority of studies in literature which have failed to find any correlation.

The need for assisted ventilation has also been found to be a significant prognostic factor in our study which is in accord with the prognostic studies of both NK Singh et al[63] and Winer et al.[61]

Other possible prognostic factors analysed in this study were severity of

muscle weakness at peak, presence of objective sensory loss, sphincter disturbance, cranial nerve paralysis and autonomic dysfunction. However, none of the above parameters were found to be statistically significant. The study by NK Singh et al[63] shows similar results with severity of paralysis at peak, adversely affecting outcome in the patients. However, his study shows that presence of bulbar paralysis is also associated with a poor prognosis. In our study, although out of 18 patients with cranial nerve paralysis, four had a bad outcome, the association with outcome is not found to be significant.

In summary, delayed onset of recovery from paralysis, requirement of mechanical ventilatory support are significant prognostic factors of outcome in GBS.

The drawbacks of our study were incomplete follow-up of 5 patients due to patient drop out.

CONCLUSIONS

1. GBS occurs in all age groups with a greater incidence in the older age group above 40 years. However age does not have any correlation with prognosis.

2. GBS affects both sexes; however males are affected more than females in the ratio of 11:04.

3. Upto 2/3rds of patients report a definite antecedent event prior to onset of GBS.

4. Onset of GBS is heralded by sensory symptoms in the majority of patients. However, objective sensory deficit is seen in very few patients.

5. Ascending type of paralysis is most commonly seen in GBS with a predominant proximal muscle weakness.

6. Progression to maximal motor deficit occurs within 2 weeks in 90% of patients. Progression of muscle weakness beyond 4 weeks is not seen.

7. Respiratory failure occurs in l/3rd of patients in GBS.

8. Autonomic dysfunction is very common in GBS. But is has no correlation with prognosis.

9. Cranial nerve dysfunction occurs in 60% of patients in GBS. Facial nerve is most commonly involved.

10. Albuminocytological dissociation is seen in majority of patients of GBS after 1 week. However, CSF protein level has no prognostic value.

11. Rapid progression from onset to peak paralysis, prolonged duration of peak paralysis, need for ventilatory support and severity of paralysis are the factors associated with poor prognosis in GBS.

12. Nerve conduction study results consistent with axonal pattern and mixed pattern of neuropathy are associated with poor prognosis.

13. Mortality in GBS is 13%.

STATISTICAL METHODS APPLIED

Following statistical methods were applied in the present study

1. Cross tabs procedure (Contingency coefficient test)
2. Chi-square test
3. Descriptive statistics

A brief description of each statistical method is given below

Crosstabs procedure

The Crosstabs procedure forms two-way and multiway tables and provides a variety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use.

Crosstabs' statistics and measures of association are computed for two-way tables only. If you specify a row, a column, and a layer factor (control variable), the Crosstabs procedure forms one panel of associated statistics and measures for each value of the layer factor (or a combination of values for two or more control variables). For example, if GENDER is a layer factor for a table of MARRIED (yes, no) against LIFE (is life exciting, routine, or dull), the results for a two-way table for the females are computed separately from those for the males and printed as panels following one another.

Chi-square test

The Chi-Square Test procedure tabulates a variable into categories and computes a chi-square statistic. This goodness-of-fit test compares the observed and expected frequencies in each category to test that all categories contain the same proportion of values or test that each category contains a user-specified proportion of values.

Descriptive Statistics

Provides summary information about the distribution, variability, and central tendency of a variable.

All the statistical operations were done through SPSS for Windows Evaluation Version 14, (SPSS Inc. New York).

BIBLIOGRAPHY

1. Robert M passcuzzim, MD, and James D. Fleck, MD: Acute peripheral neuropathy in adults; Guillain Barre Syndrome and related disorders: Neurolgy clinics Vol 15: 529 - 547.
2. Guillain G, Barrc JA, Strohi A. Sur un syndrome de radiculoncuritc avce hyperalbuminsc du liquids cephalorachidicn sans reaction celtare. Bullern dc la Societe de Medicine de L'Hospital de Pan's (translation in Archieves of Neurology 1968, 18, 450-452) 1916, 40: 1462-1470.
3. Haymaker W, Kcrnohan JW. The Landry-Guillain-Barre syndrome. A clinicopathologic report of fifty fatal cases and a critique of the literature. Medicine 1949; 28: 59- 141.
4. Fisher CM: An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). N Engl J Med 255; 57 - 65, 1956.
5. Asbury AK, Arnason BG, Adams RD. The inflammatory lesion in idiopathic polyneuritis. Medicine 1969; 48: 173- 15.
6. Griffin JW, Li CY, Ho TW, et al. Guillain-Barre syndrome in northern China: the spectrum of neuropathologic changes in clinically defined cases. Brain 1955; 118:577-595.
7. HO TW, Mishu B, Li Cy, et al. Guillain-Barre Syndrome in Northern China: Reltionship to Campylobacter jejuni infection and nti-Glycolipid Antibodies. Brain 1955; 118: 597-605.

8. Griffin JW, Li Cy, HoTW, et al. Pathology of the motor-sensory axonal Guillain-Barre syndrome. Ann Neurol 1996; 39: 17-28.
9. Waksman BH, Adams RD: Allergic neuritis: An experimental disease of rabbits induced by the injection of peripheral nervous tissue and adjuvants. J Exp Med 102:213-235, 1955.
10. Hartung HP, Pollard JD, Harvey GK, et al: Immunopathogenisis and treatment of the Guillain-Barre syndrome Part 1. Muscle Nerve 18: 137 - 153, 1995.
11. Hartung HP, Pollard JD, Harvey GK, et al: Immunopathogenesis and treatment of the Guillain-Barre syndrome Part II. Muscle nerve 18: 154 - 164, 1995.
12. Hartung HP, Hughes RAC, Taylor WA, Heininger K, Reiners K, Toyke KV: T-Cell activation in Guillain-Barre syndrome and in MS: elevated scrum levels of soluble IL-2 receptors. Neurology 1990; 40: 215 - 218.
13. Osterman PO, Lundcmo G, Pirskanen R, et al. Beneficial effects of plasma exchange in acute inflammatory polyradiculoneuropathy. Lancet 1984; 2: 1296- 1298.
14. Hafer-Macko CE, Sheikh KA, Li CY, Ho TW, et al. Immune Attack on the Schwann Cell Surface in Acute Inflammatory Demyelinating Polyneuropathy. Ann Neurol 1996; 39: 625 - 635.

15. Luijtcn JAFM, Baart dc Faille-Kuyper EH. The occurrence of IgM and complement factors along myelin sheaths of peripheral nerves: an Immunohistochemical study of the Guillain-Barre syndrome. Preliminary communication. J Neurol Sci 1972; 15: 219 - 224.
16. Barry GW Arnason and Betty Soliven: Acute Inflammatory Demyelinting Polyradiculoneuropathy: Arch Neurol 1985; 42: 1437 - 1480.
17. Oomes PG, Jacobs BC, Hazenberg et al: AntiGMl IgG antibodies and Campyolbactcr bacteria in Guillain-Barre syndrome: Evidence of molecular mimicry. Ann Neurol 1995; 38: 170- 175.
18. Vreisendrop FJ, Mishu B, Blaer M, ct al: Serum antibodies to GM1, peripheral nerve myelin, and Campylobacter jejuni in patients with Guillain-Barre syndrome and controls. Ann Neurol 34: 130 - 135, 1993.
19. Willison HJ, Veitch J, Patterson G, ct al: Miller Fisher syndrome is associated with serum antibodies to GQlb ganglioside. J Neurol Neurosurg Psychiatry, 1993; 56204-206.
20. Schonberger LB, Hurwitz ES, Katona P et al. Guillain - Barre syndrome its peidemiology and association with influenza vaccination. Ann. Neurol. 1981; 9:31-38.
21. Ropper AH: The Guillain-Barre syndrome. N Engl. J Med 1992; 326:1130 -1136.

22. Barry GW Arnason and Betty Soliven: Acute inflammatory Demyleinating Polyradiculoneuropathy. Dyck, Thomas, Griffin, Low, Poduslo: Peripheral Neuropathy, Vol 2; 3rd Edition, Pg 1437 - 1478.
23. Kurtland LT, Wiederhott WC, Kirkpatrick J, Potter HG, Armstrong P. Swine Influenza Vaccine and Guillain Barre syndrome: epidemic or artifact? Arch Neurol 1985; 42: 1089- 1090.
24. Vinkcn PJ, Bruyn GW, Klawans HL: Handbook of clinical Neurology, Vol 47: Demyelinating diseases; Guillain-Barre syndrome: 608 - 612.
25. Fisher JR. Guillain Barre syndrome following organophosphate poisoning. J Am Med Assoc 1977; 238: 1950- 1951.
26. Adlakha A, Philip PJ, Dhar KL. Guillain Barre syndrome as a sequela of organophosphorous poisoning. J Assoc Phys India 1987; 35: 665 - 666.
27. Roppcr AH. Pain in Guillain Barre syndrome. Arch Neurol, 1984;4:511-514
28. Zochodnc DW. Autonomic involvement in Guillain-Barre syndrome: a review. Muscle Nerve 1994; 17: 1145 - 1155.
29. Ropper AH. Unusual Clinical variants and signs of Guillain Barre sydrome. Arch Neurol, 1986; 43: 1150- 1152.
30. Ropper AH, Wijdicks EFM, Shahani BT. Electrodiagnostic abnormalities in 113 patients with Guillain-Barre syndrome. Arch Neurol 1990;47:881-887.

31. Sumher AJ. The physiological basis for symptoms in Guillain-Barre syndrome. Ann Neurol 1981; 9: 28 - 30.
32. Miller RG, Peterson GW, Daublc JR, et al:Prognostic value of electrodiagnosis in Guillain-Barre syndrome. Muscle Nerve 1988; 1:769- 774.
33. McKhann GM, Griffin JW, Cornblath DR, et al: Plasmapheresis and Guillain-Barre syndrome: Analysis of prognostic factors and the effect of plasmapheresis. Ann Neurol 1988; 23: 347 - 353.
34. Triggs WJ, Cros D, Gominak SC, et al: Motor nerve inexictability in Guillain-Barre syndrome. Brain 115: 1291 - 1302, 1992.
35. Asbury AK, Arnason BG, Karp HR, McFarlin DE. Criteria for diagnosis of Guillain-Barre syndrome. Ann Neurol 1978; 3: 565 - 566.
36. Asbury Ak, Cornblath DR. Assessment of current Diagnostic criteria for Guillain-Barre syndrome. Ann Neurol 1990; 7(Suppl): S21 - 24.
37. Aleem MA. Intravenous immunoglobin in specific neurological diseases. Neurosciences today Mediworld Publications Group. 1999;3(4): 192 - 202.
38. Guillain-Barre study Group. Plasmapheresis in acute GBS. Neurology 1985; 35: 1096- 104.
39. Blettle RP, Gross M, Legg NJ et al. Treatment of acute polyneuropathy by plasma exchange. Lancet 1978; 2: 1100.

40. Guillain Barre study Group. Plasnaogeresus and acute GBS. Neurology 1984; 35: 1096- 104.
41. Hughes RAC, Newsom-Davis JM, Perkin GD, et al. controlled trials of prednisolone in acute polyneuropathy. Lancet 1978; 2: 1100.
42. Pangariya A, Sharma B, Sardana V. High Dose Methyl Prednisolone therapy in guillain-Barre syndrome. Neurosciences today 1997; 1 (2): 151—154.
43. Tharton CA, Girggs RC. Plasma exchange and infravenous immunoglobin treatment of neuromuscular disease. Arnals of neurology 1994; 35(3): 260 -68.
44. Castro LHM, Ropper AH. Human immune globulin infusion in Guillain-Barre syndrome Neurology 1996; 46: 100 - 3.
45. Geeta A Khwaja. Management strategies in Guillain-Barre syndrome. Neuroscicnccs today 2001; 5: 22 - 32.
46. Vander Mccfhe, Van Doom PA. Guillain-Barre syndrome and chronic inflammatory demyelinating polyneuropathy; immune mechanisms and update on current therapies. Ann Neurol 1995; 37: 514-31.
47. Haupt WF, Roscnow F, Vanderven C, et al. Sequential treatment of Guillain-Barre syndrome with extracorporeal elimination and intravenous immunoglobulin. J Neurol Sci 1996; 137: 145-49.

48. Plasma Exchange/Sandoglobulin Guillain-Barre syndrome Trial group. Randomised trial of plasma exchange, intravenous immunoglobulin and combined treatments in Guillain-Barre syndrome. Lancet 1997;349:225-30.

49. Thanakan J, Jayaprakash PA, ct al. Small volume plasma exchange in GBS. Experience in 5 patients. JAPI 1990; 38: 550 - 554.

50. Hughes RAC, Winer JB. Guillain-Barre syndrome Recent advances in clinical Neurology 1984; chapter 2; pg 19 - 49.

51. Hughes RAC. Ineffectiveness of high dose intravenous methyl prednisolone in Guillain-Barre syndrome. Lancet 1991; 338: 1142.

52. Feasby TE. Acute GBS. Peripheral nerve disorders. Current therapy in neurologic disease. Editurs: Richard T Johnson Mosy. Year Book 1993, 347 -349.

53. Roy T, Roy O, Basu S Respiratory Dysfunction in acute GBS. Prog Clin Neurosciences 1996; 11: 199-207.

54. Zou LP, Zhu J, et al treatment will P2 protein peptide 57-81 by nasal route in effective in Lewis fat experimental autoimmune ncuritirs. J Neuroimmunol 1998: 89: 137-45.

55. Nicoletti F, Nicletti A, Guiffrida S, et al. Sodium Fusidatc in Guillain-Barre syndrome J Neurol Ncurosurg Psychiatr 1998; 65: 266 - 68.

56. Winer JB, Hughes RAC, Greenwood RJ, et al: Prognosis in Guillain-Barre syndrome. Lancet, 1985; 1: 1202- 1203.

57. Chowdhury D, Rohatgi A, SNA Rizvi, NP Singh: Current concepts of diagnosis, management and prognosis of Guillain-Barre syndrome. JAP1, 1997; 45:205-210.
58. RHM Hadden, RAC Hughes: Guillain-Barre syndrome: Recent advances, J Applied Medicine 1998; 563 - 568.
59. Osier ID, Sidell AD. The Guillain-Barre syndrome: the need for exact diagnostic criteria. N Engl J Med, 1960; 262: 964 - 969.
60. Marshall J. The Landry-Guillain-Barre syndrome. Brain 1963; 86: 56 - 66.
61. Winer JB, Hughes RAC, Osmond C. A prospective study of acute idiopathic neuropathy: Clinical features and their prognostic value. J Neurol, Neurosurg, Psychiatry, 1988;51:605-612.
62. Eberle E, Brink J, Azen J, White D. Early predictors of incomplete recovery in children with Guillain-Barre polyneuritis. J Pediatr 1975; 86: 356 - 359.
63. Singh NK, AK Jaiswal, S Misra, PK Srivastava: Prognostic factors in Guillain-Barre syndrome. J Assoss Phys India 1994; 42: 777 - 779.
64. Recs JH Soudain, Gregson NA, Hughes RAC: A prospective case control study to investigate the relationship between Campylobacter jejuni infection and Guillain-Barre syndrome. A Engl J Med 1995; 333: 1374 - 1379.
65. Peter C Dowling, Joseph P Mennona, Stuart D Cook. Guillain-Barre

syndrome in Greater New York-New Jersey. J Am Med Associ 1977; 238: 317 - 318.

66. Robert M. Eiben, Welton M. Gcrsony. Recognition, prognosis and treatment of Guillain-Barre syndrome. Med Clinics of N Am 1963: 1371 - 1380.
67. Kaur U, Choupra JS, Prabhakar S, Radhakrishnan K: Guillain-Barre syndrome - A clinical electrophysiological and biochemical study. Aeta Neurol Scandinavica 1986: 73: 394-402.
68. Flachcnecker P, Wermuth P, Hartung H-P, Reiners K. Quantitative assessment of cardiovascular autonomic function in Guillain-Barre syndrome. An Neurol 1997; 42: 171 - 179.
69. Wadia RS. The neurology of organophosphorus insecticide poisoning, newer findings - a view point. J Assoc Phys India 1990; 38: 129 - 131.
70. WB Mathews, Gilbert, H. Glaser. Guillain-Barrc Syndrome: Recent advances in clinical Neurology (4); Hughes RAC, Winer JB (ed), Chruchill Livingston, 1984.

PROFORMA

1) Name :
2) Date :
3) Address :
4) Age and Sex :
5) O.P. Number :
6) Date of onset :
7) Date of admission :
8) Duration before hospitalization :

PRESENTING SYMPTOMS:-

MOTOR SYMPTOMS:-

9) H/o muscle weakness in lower limbs

a) Onset	→	Sudden	☐	Insidious	☐
b) Distribution	→	Proximal	☐	Distal	☐
c) Which is first	→	Proximal	☐	Distal	☐
d) Weakness in both limbs	→	Symmetrical	☐	Asymmetrical	☐

10) H/o muscle weakness in upper limbs:

a) Onset	→	Sudden	☐	Insidious	☐
b) Distribution	→	Proximal	☐	Distal	☐
c) Which is first	→	Proximal	☐	Distal	☐
d) Weakness in both limbs	→	Symmetrical	☐	Asymmetrical	☐

11) Duration between weakness in lower limbs and weakness in upper limbs ☐ days.

12) H/o Clumsiness or falling during walking	Yes	☐	No	☐
13) H/o Trunk muscle weakness:	Present	☐	Absent	☐
14) H/o Involvement of Neck muscles:	Present	☐	Absent	☐
15) H/o Cranial nerves involvement:	Present	☐	Absent	☐

a) _____

b) _____

c) _____

d) _____

e) _____

16) H/o difficulty in breathing: Present ☐ Absent ☐

17) H/o Autonomic nervous system involvement

Bladder ☐ Bowel ☐ Sweating ☐ Postural giddiness ☐ Palpitations ☐

18) **SENSORY SYMPTOMS:**

	Upper limbs / Level	Lower limbs / Level
H/o Pains		
H/o Tingling Sensation		
H/o Numbness		

19) H/o Antecedent infection Yes ☐ No ☐

URTI ☐ UTI ☐ Malaria ☐ Viral Fever ☐

20) Any other Antecedent event Yes ☐ No ☐

Surgery ☐ HIV infection ☐ Drugs ☐ Malignancy ☐ Vaccination ☐

21) Duration between antecedent infection and onset of presenting symptoms ☐ days.

ON EXAMINATION

22) BP :- Supine : Heart rate :

Standing :

PR : RR :

O2 Saturation :

23) **MOTOR SYSTEM**

a) Nutrition :

b) Tone : UL ☐ LL ☐

c) Muscle power (MRC) grading) :

	Neck Muscles	Upper Limbs		Trunk	Lower Limbs	
		Proximal	Distal		Proximal	Distal
Right						
Left						

D) Reflexes:

Superficial Reflexes

	Corneal	Conjuctival	Abdominal	Cremasteric	Plantars
Right					
Left					

E) Deep Reflexes

	Biceps	Triceps	Supinator	Knee jerk	Ankle jerk
Right					
Left					

SENSORY SYSTEM:

1) Upper limbs:

	Pain	Temp	Light Touch	Joint Position	Vibration
Right					
Left					

2) Lower limbs:

	Pain	Temp	Light Touch	Joint Position	Vibration
Right					
Left					

25) **INVESTIGATIONS:**

a) ECG :

b) Serum Electrolytes : Na + K+

c) CSF Analysis at after _____ days from onset

Protein ☐ Sugar ☐ Cell count ☐

d) Nerve conduction studies after _____days from onset.

Demyelinating Type ☐ Axonal Type ☐ Mixed Type ☐

26) Treatment given

Plasmapheresis ☐ IVIG ☐ IVMP ☐ None ☐

27) Duration of hospitalization_____ days.

28) Out Come_____

29) Hughes Staging At admission ☐

At Peak ☐

At 3 months ☐

MASTER CHART

						PATTERN OF EVOLUTION OF WEAKNESS					SENSORY SYMPTOMS			
SI. No.	HOSPITAL NO.	AGE YRS.	SEX M/F	PRO DROME +/-	NUMBER OF DAYS PRIOR TO DOO	A/D/S	P-D OR D-P	CRANIAL NERVES		RESP. PARALYSIS +/-	SUBJECTIVE +/-	OBJECTIVE	AUTONOMIC DYSFUNCTION +/-
								RT.	LT.				
1	12834	37	M	-	-	A	P-D	7	7	-	+	-	+
2	13651	23	M	-	-	A	P-D	0	0	-	+	Touch	-
3	14026	58	M	+	3	D	P-D	0	0	-	-	-	-
4	14861	54	M	-	-	S	P-D	3,4,6, 7,9,10	3,4,6, 7,9,10	-	+	-	+
5	15326	26	M	+	8	D	D-P	0	0	-	-	-	-
6	15931	40	M	+	10	A	S	7	7	-	+	Joint Position	-
7	16123	42	M	-	-	D	D-P	0	0	-	-	-	-
8	17821	67	M	+	3	A	D-P	0	0	+	+	-	+
9	18236	20	M	-	-	A	P-D	0	0	-	+	-	+
10	19312	32	F	-	-	A	D-P	7	7	-	+	-	+
11	20856	55	M	-	-	A	P-D	7	7	+	+	-	-
12	21732	30	M	+	12	A	P-D	0	0	+	+	-	-
13	22913	59	F	+	8	A	D-P	9,10	9,10	+	+	-	-
14	24312	12	M	+	20	D	D-P	7	0	-	-	-	+
15	26139	62	F	-	-	A	P-D	7,12	0	-	+	Touch Vibration	+
16	28300	34	F	+	9	A	D-P	7	7	+	+	-	+
17	28912	53	M	+	7	A	S	7,9,10	7,9,10	+	+	-	+
18	30123	23	M	+	2	A	P-D	0	0	-	+	-	+
19	33392	45	F	+	16	S	S	7	7	-	+	-	-
20	33931	40	F	-	-	S	P-D	0	0	-	-	-	+
21	34391	40	M	-	-	D	P-D	0	0	-	-	-	-
22	35161	47	M	+	14	A	P-D	7	7	-	+	-	-
23	35571	47	M	+	8	A	D-P	7,9,10	7,9,10	+	+	-	+
24	35902	65	M	+	7	A	P-D	0	0	-	+	-	-
25	36131	29	F	-	-	A	D-P	7	7	-	+	-	-
26	37123	55	M	+	10	A	P-D	0	0	+	+	-	-
27	38391	29	F	+	14	A	P-D	7,9,10,11	7,9,10	+	-	-	-
28	40130	30	F	+	6	A	P-D	7	7	-	+	-	+
29	40936	22	M	+	6	A	P-D	7,9,10	7,9,10	+	+	-	+
30	41784	13	M	-	-	A	S	7	7	-	-	-	-

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No : 044 25305301
Fax: 044 25363970

CERTIFICATE OF APPROVAL

To

Dr.D.Ganesa Pandian,
Postgraduate in Neurology,
Institute of Neurology,
Madras Medical College, Chennai-3.

Dear **Dr.D.Ganesa Pandian,**

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "**Analysis of Clinical, Investigatory Profile in the Management and Outcome of Gullain-Barrè Syndrome"** No.31042014.

The following members of Ethics Committee were present in the meeting held on 08.04.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C.Rajendran, M.D,	-- Chairperson
2.	Prof. Kalaiselvi, M.D, Vice Principal, MMC, Ch-3	-- Member Secretary
3.	Prof. Nandhini, M.D, Inst. of Pharmacology, MMC, Ch-3	-- Member
4.	Prof.Bhavani Sankar, M.S, Prof & HOD General Surgery, MMC, Ch-3	-- Member
5.	Prof.V.Padmavathi, M.D, i/c. Director of Pathology, MMC, Ch-3	-- Member
6.	Thiru. Rameskumar Administrative Office, MMC, Ch-3.	-- Lay person
7.	Thiru. Govindasamy, B.A., B.L., Lawyer, ~~Ch.~~	-- Lawyer
8.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

15/4/14

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

15/4/14

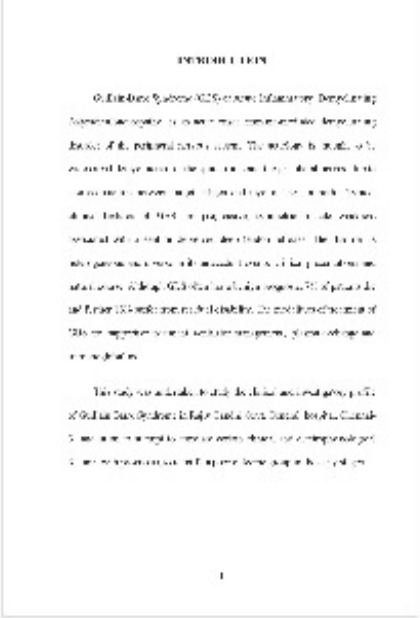
turnitin

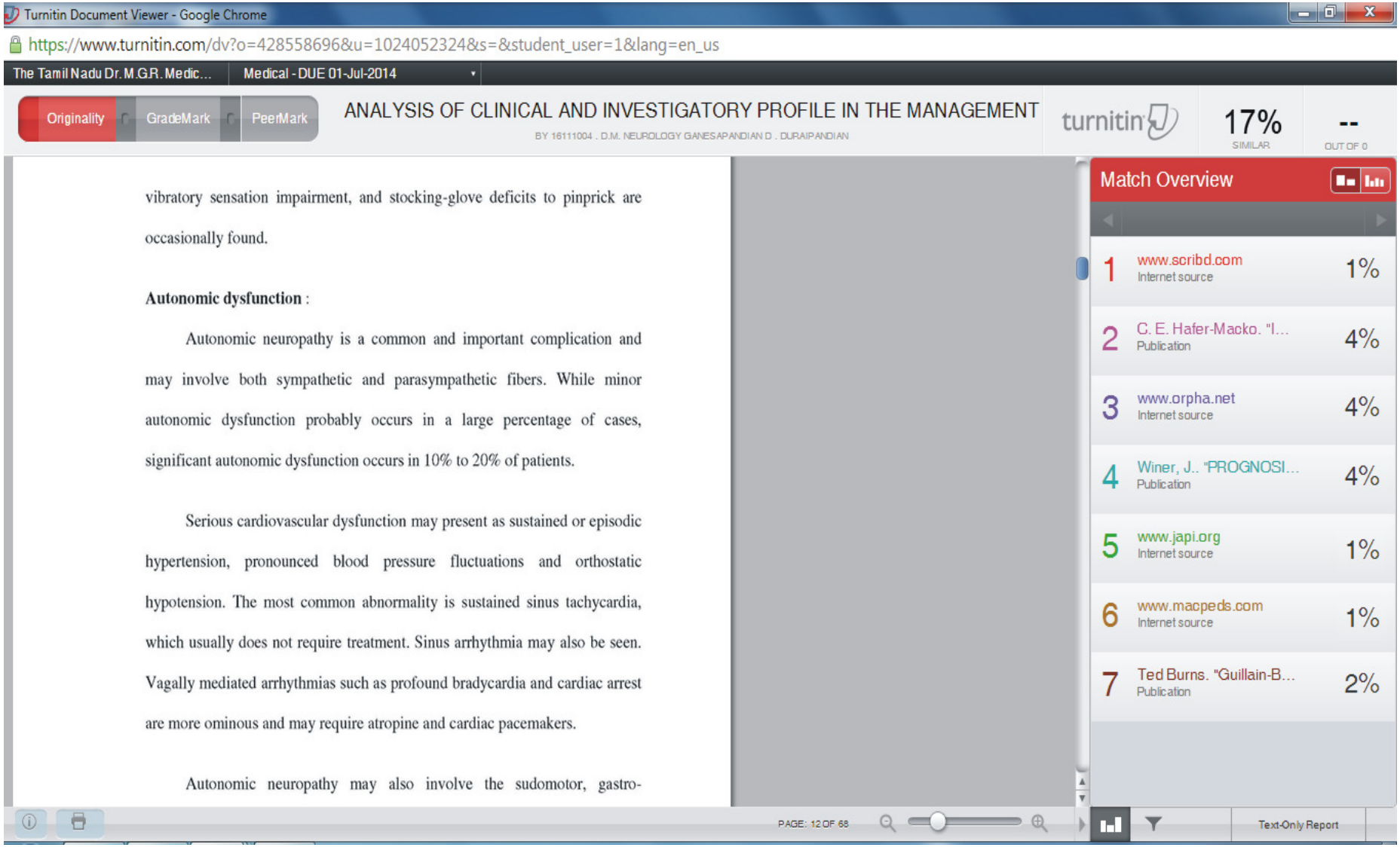
Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	16111004 . D.m. Neurology GANESA..
Assignment title:	Medical
Submission title:	ANALYSIS OF CLINICAL AND INVES..
File name:	LE_IN_THE_MANAGEMENT_AND_O.
File size:	6.76M
Page count:	68
Word count:	568
Character count:	3,379
Submission date:	19-May-2014 12:48PM
Submission ID:	428558696




Turnitin Document Viewer - Google Chrome
https://www.turnitin.com/dv?o=428558696&u=1024052324&s=&student_user=1&lang=en_us
The Tamil Nadu Dr. M.G.R. Medic...
Medical - DUE 01-Jul-2014
Originality
GradeMark
PeerMark
ANALYSIS OF CLINICAL AND INVESTIGATORY PROFILE IN THE MANAGEMENT
BY 16111004 . D.M. NEUROLOGY GANESAPANDIAN D . DURAIPANDIAN
turnitin
17%
SIMILAR
--
OUT OF 0
vibratory sensation impairment, and stocking-glove deficits to pinprick are occasionally found.
Autonomic dysfunction :
Autonomic neuropathy is a common and important complication and may involve both sympathetic and parasympathetic fibers. While minor autonomic dysfunction probably occurs in a large percentage of cases, significant autonomic dysfunction occurs in 10% to 20% of patients.
Serious cardiovascular dysfunction may present as sustained or episodic hypertension, pronounced blood pressure fluctuations and orthostatic hypotension. The most common abnormality is sustained sinus tachycardia, which usually does not require treatment. Sinus arrhythmia may also be seen. Vagally mediated arrhythmias such as profound bradycardia and cardiac arrest are more ominous and may require atropine and cardiac pacemakers.
Autonomic neuropathy may also involve the sudomotor, gastro-
Match Overview
1 www.scribd.com Internet source 1%
2 C. E. Hafer-Macko. "I... Publication 4%
3 www.orpha.net Internet source 4%
4 Winer, J.. "PROGNOSI... Publication 4%
5 www.japi.org Internet source 1%
6 www.macpeds.com Internet source 1%
7 Ted Burns. "Guillain-B... Publication 2%
PAGE: 12 OF 68
Text-Only Report